SOT

SAN ANTONIO

March 11–15, 2018

57th Annual Meeting and ToxExpo™

Preliminary Program

Dear Colleagues:

On behalf of the SOT Council, Committees, Exhibitors, Regional Chapters, Special Interest Groups, Specialty Sections, Supporters, and other partners, I invite you to join us in San Antonio, Texas, March 11–15, 2018, for the SOT 57th Annual Meeting and ToxExpo.

Every year, SOT prides itself on hosting the preeminent toxicology conference in the world, providing access to groundbreaking, basic, and applied science. More than 2,000 presenters will be sharing their research and expertise during the 170+ Scientific Sessions, featuring more than 2,500 abstracts.

Based on feedback from our members and meeting attendees, we are excited to announce a new all-day Poster Session format for 2018. We believe this will enhance the experience of all attendees who in the past may not have been able to visit posters due to conflicting schedules.

With more than 6,500 toxicologists from all over the world expected to attend, opportunities for networking and finding new collaborators are abundant—from the Scientific Sessions and other daytime events through the evening receptions. To help attendees make connections, once again, we have created dedicated networking time on Tuesday and encourage you to visit with the 330+ ToxExpo exhibitors during this time. As always, ToxExpo is hosting leading organizations, companies, laboratories, agencies, research partners, and more, ready to provide information on new products and technology, career and partnership opportunities, and other toxicological research-related support.

SOT is delighted to be returning to San Antonio for the first time since 2013. The newly renovated Henry B. González Convention Center is located near the River Walk, adjacent to Hemisfair Park, and a short walk to the Alamo, Spanish Missions, and Market Square.

I hope you join us in the heart of Texas for the 57th Annual Meeting and ToxExpo to help explore, advance, and understand the field of toxicology.

Sincerely,

Patricia E. Ganey, PhD
2017–2018 SOT President

SOT
★2018 San Antonio★

57th Annual Meeting and ToxExpo

March 11–15, 2018

SOT Mobile Event App!

An interactive version of the SOT *Program*, *The Toxicologist*, ToxExpo, and more.

Connect with fellow attendees, speakers, and exhibitors.

Build a personalized schedule that also syncs with the computer-based Online Planner (available in January).

View and Search for Scientific Sessions, abstracts, and ePosters.

Access Convention Center and San Antonio maps.

Navigate the ToxExpo floor plan and find products and services.

Engage with SOT online (Blog, ToXchange, Facebook, Twitter).

Available for download in February 2018 from all the major app stores.

To purchase an advertisement on the SOT Mobile Event App, please visit to **www.toxexpo.com**.

Download on the App Store

GET IT ON Google Play

Dear Colleagues,

The 2018 Annual Meeting and ToxExpo will showcase the very best in toxicological science with Scientific Sessions featuring leading experts from across the broad range of disciplines and specialties that inform and advance toxicology. Beyond presenting these sessions that capture cutting-edge research and discoveries in toxicology, this year's program also features several sessions focused on the application of our science to illustrate the impact of toxicology research on human and environmental health. There are four sessions with the designation Innovations in Applied Toxicology (IAT) or Innovations in Toxicological Sciences (ITS), and we hope you will attend one of these dedicated sessions.

We are delighted that Matthew H. Porteus, Stanford University, will be presenting this year's Opening Plenary Session on gene editing and that the keynote Medical Research Council (MRC) lecture on circadian rhythms will be delivered by Michael Hastings, MRC Laboratory of Molecular Biology.

Another exciting new development for 2018 will be the introduction of all-day Poster Sessions. Posters will be displayed all-day in the ToxExpo Exhibit Hall with the presenting authors available for questions and discussions during one of four 90-minute blocks. The assigned attendance times will be available in the final *Program* and in the SOT Mobile Event App. We anticipate that this change will allow you to experience more science than ever at the meeting.

In San Antonio, SOT is pleased to continue and enhance its special partnership with two sister toxicology associations. SOT and the Japanese Society of Toxicology (JSOT) are expanding their joint Special Symposium Session to 165 minutes, and it will feature four presenters (two from SOT and two from JSOT) discussing environmental neurodevelopmental risk. Then, in addition to the annual SOT/EUROTOX debate, which will feature the question of whether adverse outcome pathways are the future for regulatory toxicology, SOT and EUROTOX will be exchanging award lecturers for the first time in 2018. Vera Rogiers, Vrije Universiteit Brussel, will be presenting the EUROTOX Bo Holmstedt Memorial Award Lecture on Wednesday morning, and Robert J. Kavlock will be presenting the SOT Merit Award Lecture at our meeting and at EUROTOX 2018.

Alongside these new sessions will be SOT trademark events, such as the Meet the Directors session, featuring Linda S. Birnbaum, National Institute of Environmental Health Sciences (NIEHS); Mark S. Johnson, Tri-Service Toxicology Consortium; and Edward J. Perkins, Army Corps of Engineers Environmental Laboratory; and special lectures by the recipients of the SOT Distinguished Toxicology Scholar and SOT Translational Impact Awards.

You can still add your science to the program by submitting a late-breaking abstract by January 12, 2018. The submission fee for late-breaking abstracts is $75. More information on submitting a late-breaking abstract is available on page 119 and online at www.toxicology.org/2018.

Please join me and the rest of the Scientific Program Committee in San Antonio for the latest news and advancements in toxicology.

Warmest regards,

Leigh Ann Burns Naas, PhD, DABT, ATS, ERT
SOT Vice President and Scientific Program Committee Chairperson, 2017–2018

SOT 2018 San Antonio

Preliminary Program Content Reference Guide

Preliminary Program Overview

Section	Description
Scientific Program Overview (pages 6–9)	This calendar provides a daily listing of Annual Meeting sessions with their scheduled dates and times, including Symposia, Workshops, and Roundtables, special lectures, and Platform and Poster Sessions. Please refer to the final *Program*, SOT Mobile Event App, or Annual Meeting website for detailed information.
Events and Activities (pages 40–55)	The 57th Annual Meeting events and activities details are provided in this section, including the Regional Chapter, Special Interest Group, and Specialty Section reception schedules; Student and Postdoctoral Scholar Events; and Undergraduate Diversity and Education Programs.
Continuing Education (pages 56–66)	Continuing Education (CE) course descriptions and presenter information are located in this section. These courses have separate registration fees. Each participant in a CE course will receive a digital copy of the course book. Any remaining digital copies (available on USB drives) can be purchased by meeting attendees beginning Monday, March 12, while supplies last.
Featured Sessions (pages 69–73)	This section lists the Plenary Sessions and other special lectures and Scientific Sessions for the 2018 Annual Meeting. Detailed information for these sessions will be available in the final *Program* and SOT Mobile Event App.
Scientific Sessions (pages 75–118)	The *Preliminary Program* layout is similar to that of the final *Program*. Specifically, this section lists the Scientific Sessions in date, time, and alphabetical order for Symposium, Workshop, Roundtable, Informational, Education-Career Development, Historical Highlights, and Regional Interest Sessions.
ToxExpo Exhibits (pages 120–132)	ToxExpo is the profession's largest exposition and best resource for the latest information in technology, equipment, and services. This section contains the current list of exhibiting companies and Exhibitor-Hosted Sessions. Up-to-date information is available at www.ToxExpo.com and will be in the SOT Mobile Event App.

Session Types

Education-Career Development Sessions (80 minutes)—Provide tools and resources to toxicologists that will enhance their professional and scientific development (throughout pages 75–118)

Exhibitor-Hosted Sessions (60 minutes)—Developed by a ToxExpo Exhibitor or Annual Meeting Supporter (starting on page 124)

Featured Sessions (Timing Varies)—Plenary, Keynote, and other special sessions (starting on page 69)

Historical Highlights Sessions (80 or 165 minutes)—Provide a review of a historical body of science that has impacted toxicology (throughout pages 75–118)

Informational Sessions (80 or 165 minutes)—Present the latest science in toxicology or other learning opportunities that address the professional interests and needs of toxicologists in the areas of career development, general information, and planned scientific activities and are not based on the outcome of scientific research (throughout pages 75–118)

Platform Sessions (165 minutes)—Oral presentations that cover new areas, concepts, or data (see details in the final *Program* and SOT Mobile Event App)

Poster Sessions (All Day)—Topic-specific presentations that cover new areas, concepts, or data (see details in the final *Program* and SOT Mobile Event App)

Regional Interest Sessions (165 minutes)—Central topics of relevance that describe public health and/or ecological problems related to a region (throughout pages 75–118)

Roundtable Sessions (80 minutes)—Provide an overview of controversial subjects, followed by questions and discussion (throughout pages 75–118)

Symposium Sessions (165 minutes)*—Cutting-edge science, emphasizing new areas, concepts, and data (throughout pages 75–118)

Workshop Sessions (165 minutes)*—Generally accepted, state-of-the-art knowledge in toxicology in informal interactive presentations with ample time for discussion (throughout pages 75–118)

Subdesignation of Symposium and Workshop Sessions

Innovations in Applied Toxicology Session—This symposium or workshop subcategory demonstrates innovation in applied toxicology and how the topic may impact the practice of toxicology **IAT**

Innovations in Toxicological Sciences Session—This symposium subcategory introduces new technologies or scientific disciplines to attendees **ITS**

Sunday, March 11

7:00 AM to 7:45 AM

CONTINUING EDUCATION SUNRISE MINI-COURSES

SR01 CRISPR-Cas9 for Toxicologists

SR02 The What, When, and How of Using Data from Alternative Testing Methods in Chemical Safety Assessments

8:15 AM to 12:00 Noon

CONTINUING EDUCATION MORNING COURSES

AM03 An Introduction to the Basics of Immunotoxicity Testing

AM04 Assessment of Peri- and Prepubertal Developmental and Reproductive Toxicity

AM05 Biotherapeutic Development: What's behind the Curtain?

AM06 *In Vitro* Testing: Tales from the Real World

AM07 Physiologically-Based Pharmacokinetic Modeling to Support Modernized Chemical Safety Assessment

AM08 Developmental Neurotoxicity Testing: Current Practices and Latest Advancements

1:15 PM to 5:00 PM

CONTINUING EDUCATION AFTERNOON COURSES

PM09 Consumer Products Safety Assessment: Progress in the Use of Alternatives to Animal Models

PM10 Evaluation of Leachable Substances from Materials with Applications in Foods and Pharmaceuticals: Science- and Risk-Based Approaches

PM11 Lead Optimization of Therapeutic Small Molecules: From Drug Target to Clinical Candidate Selection—Strategies and Decision Making

PM12 NGS-Based Technologies Enable Biomarker Development and Discovery in Toxicology

PM13 Uncertainty Characterization in 21st-Century Toxicology: Current Practice and Practical Methods Supporting Regulatory Risk Assessment

PM14 Xenobiotic Pharmacokinetics during Pregnancy and Lactation

Monday, March 12

8:00 AM to 9:00 AM

PLENARY SESSION

- Developing Genome-Edited Stem Cells for Therapy of Patients: Assessing Efficacy and Toxicology
  Lecturer: Matthew H. Porteus, Stanford University

9:15 AM to 12:00 Noon

SYMPOSIUM SESSIONS

- Advanced Imaging and Microscopy for Retinal Disease and Toxicity IAT
- Cancer Risk Assessment of PAH Mixtures: Current and Future Directions
- Novel Insights on Chemical-Induced Immunotoxicity: Microvesicles and microRNA Dysregulation
- Toxicological Implication of Copper in Neurodegenerative Diseases
- Understanding the Molecular Mechanisms of Zika Virus Reproductive and Developmental Toxicity

WORKSHOP SESSIONS

- Assessing the Dose of Particles in Toxicological Studies: Advances in Dosimetry Models for *In Vitro* and *In Vivo* Applications in Light of Risk Assessment
- Predicting Drug-Induced Cholestatic Injury in Humans
- Toxicology's Next Grand Challenge: Embracing Exposure Science for Effective Public Health Protection

PLATFORM SESSION

- Investigating Mode-of-Action in Chemical Carcinogenesis

9:15 AM to 4:30 PM

POSTER SESSIONS

- Air Pollution
- Air Pollution: Ozone
- Biomarkers
- Biomarkers: RNA
- Biotransformation and Metabolism
- Cardiovascular Toxicology: Hemodynamics
- Cardiovascular Toxicology: *In Vitro* Systems
- Cardiovascular Toxicology: *In Vivo* Systems
- Food Safety and Nutrition
- Genetic Toxicity
- Immunotoxicity
- Inflammation
- Mechanistic Insights in Liver Damage
- Metals Neurotoxicology: Lead, Cadmium, and Others
- Metals Neurotoxicology: Methylmercury and Mercury
- Neurodevelopmental Toxicity I
- Neurodevelopmental Toxicity II: Autism, ASD, and Childhood Mental Disorders
- Neurotoxicology: Neurodegenerative Disease I—Alzheimers, ALS, Excitotoxicity, and Others
- New Models and Biomarkers for Liver Damage
- Ocular Toxicology
- Regulatory Policy and Policy Evaluation
- Respiratory Toxicology: *In Vitro* Studies
- Respiratory Toxicology: *In Vivo* Studies
- Safety Assessment: Drug Development
- Safety Assessment: Drug Discovery
- Understanding Kidney Damage

9:30 AM to 4:30 PM

RESEARCH FUNDING INSIGHTS

- Network with Program Officers

12:10 PM to 1:30 PM

INFORMATIONAL SESSIONS

- Changes to the Common Rule Regulations and Implications for Human Research
- Management of Toxic Wastes in Africa: Challenges and Opportunities
- Moving Beyond Theory to the Use of Systematic Review to Support Regulatory Decision Making for Evidence-Based Risk Assessment

12:30 PM to 1:30 PM

DISTINGUISHED TOXICOLOGY SCHOLAR AWARD LECTURE

- *Lecturer: Roger O. McClellan, Toxicology & Human Health Risk Analysis*

1:45 PM to 4:30 PM

SYMPOSIUM SESSIONS

- Adipocyte Toxicology and Obesogens
- Alternative Testing Strategies for Nanomaterials and Ultrafine Particles
- Chemical Grouping for 21st-Century Toxicology, Risk Assessment, and Decision Making
- Decoding Oxidative Stress from Inflammation: Implications for Exposure, Toxicity, and Disease
- Estrogen Receptor Signaling as a Mechanism of Developmental Toxicity
- High-Throughput Transcript Profiling and Functional Assessment: From Screening to Systems Biology Strategies for Personal Chemical Safety Predictions
- Revising Biology: Using Genomic and Epigenomic Editing to Gain Novel Insight into the Molecular Mechanisms of Toxic Exposure Effects and Susceptibility

REGIONAL INTEREST SESSION

- Marijuana Safety: Issues Facing the Regulatory, Medical, and Academic Environments

PLATFORM SESSION

- Mechanistic and Translational Toxicology: SPC Highlights Emerging Scientists

4:45 PM to 6:00 PM

SOT/EUROTOX DEBATE

- Adverse Outcome Pathways Are the Future for Regulatory Toxicology
  Debaters: Daniel Villeneuve, US EPA; and Brigitte Landesmann, European Commission Joint Research Centre Institute for Health and Consumer Protection

Tuesday, March 13

8:00 AM to 10:45 AM

SYMPOSIUM SESSIONS

- Clinical and Translational Toxicology: From Theory to Therapy
- Mitochondria Biogenesis and Dysfunction in Cellular Senescence in Cardiopulmonary System

WORKSHOP SESSIONS

- Advancing the Adverse Outcome Pathway Framework: An International Horizon Scanning Approach
- Computational Predictions for Dermal Penetration of Chemicals: Should More Complexity Be Considered in Addition to Simple Passive Diffusion?
- Defining Domains of Applicability for Zebrafish within Toxicology: A Retrospective and Prospective Workshop
- Get the Lead Out: The Persistent Problem of Lead Exposure from Soil, Dust, and Water
- Nanotoxicology, State of the Science, and the Path Forward

PLATFORM SESSIONS

- Chemical and Biological Weapons
- Immunotoxicity

9:15 AM to 4:30 PM

POSTER SESSIONS

- AH Receptor
- Air Pollution: Biomass
- Air Pollution: Particulate Matter
- Alternatives to Mammalian Models I
- Apoptosis and Cell Death
- Autoimmunity/Hypersensitivity
- Bioinformatics and *In Silico* Modeling
- Carcinogenesis I
- Carcinogenesis II
- Chemical and Biological Weapons
- Computational Approaches in Safety Assessment
- Computational Tools for Safety Assessment
- Developmental Basis of Adult Disease
- Ecotoxicology
- Emerging Technologies
- Endocrine Toxicology
- Epidemiology and Human Population Evaluation
- Epigenetics
- Exposure Assessment: Applications
- Exposure Assessment: Tools and Methods Development
- Gene Regulation and Signal Transduction
- Medical Devices
- Metals Neurotoxicology: Manganese
- Metals: Arsenic, Lead, and Manganese
- Mixtures
- Neurotoxicology: Neurodegenerative Disease II—Parkinson's Disease and Dopaminergic Toxicity
- Oxidative Injury and Redox Biology
- Persistent Organic Pollutants
- Pesticide Neurotoxicology
- Pesticides
- Receptors
- Reproductive Toxicology I
- Reproductive Toxicology II
- Stem Cell Biology and Toxicology
- Systems Biology
- Translational Toxicology

9:30 AM to 4:30 PM

RESEARCH FUNDING INSIGHTS

- Network with Program Officers

11:00 AM to 12:00 Noon

MEET THE DIRECTORS

- A Conversation with Linda S. Birnbaum, Mark S. Johnson, and Edward J. Perkins
  Panelists: Linda S. Birnbaum, NIEHS; Mark S. Johnson, US Army Public Health Center; and Edward J. Perkins, US Army Engineer Research and Development Center



TRANSLATIONAL IMPACT AWARD LECTURE

- *Lecturer: Jia-Sheng Wang, University of Georgia*

11:00 AM to 12:20 PM

ROUNDTABLE SESSION

- Alternative Toxicology Approaches to Evaluate Next-Generation Nicotine Products

HISTORICAL HIGHLIGHTS SESSION

- Arsenic, a Gift and Malice: From Discovery to Detrimental Effects, a Historical Perspective

EDUCATION-CAREER DEVELOPMENT SESSION

- In It to Win It: How to Negotiate During the Interview Process

12:30 PM to 1:30 PM

MERIT AWARD LECTURE

- *Lecturer: Robert J. Kavlock*

1:30 PM to 4:15 PM

SYMPOSIUM SESSIONS

- Application of Data from New Approaches in Regulatory and Product Safety Decisions
- Effectively Leveraging Cellular Functional Genomics Strategies for Elucidating Chemical Mechanisms of Action
- Stressors from Within: Neuroendocrine Regulation of Air Pollution-Induced Pulmonary and Systemic Health Effects **ITS**

WORKSHOP SESSIONS

- Big Data in Toxicology: How to Achieve Transparency and Reproducibility
- Mitochondria: Critical Targets in Pharmaceutical and Environmental Toxicity
- Safety Evaluation of Plant-Based Color Additives Used in Foods

REGIONAL INTEREST SESSION

- Communicating Science: Unconventional Oil and Gas Operations as a Case Study

HISTORICAL HIGHLIGHTS SESSION

- Radiation Toxicity: Historical Perspective on Epidemiological and Experimental Evidence Informing Standards

PLATFORM SESSION

- Persistent Organic Pollutants

4:30 PM to 5:50 PM

EDUCATION-CAREER DEVELOPMENT SESSION

- Perfecting Your "Elevator Speech"

4:30 PM to 6:15 PM

SOT ANNUAL BUSINESS MEETING

- SOT Members are encouraged to attend.

Wednesday, March 14

8:00 AM to 10:45 AM

SOCIETY OF TOXICOLOGY AND JAPANESE SOCIETY OF TOXICOLOGY SYMPOSIUM

- Environmental Neurodevelopmental Risk
  Lecturers: Yoichiro Kuroda, Environmental Neuroscience Information Center; Susan L. Schantz, University of Illinois at Urbana-Champaign; Satoshi Kitajima, National Institute of Health Sciences; and Deborah A. Cory-Slechta, University of Rochester Medical Center




WORKSHOP SESSIONS

- Cardiovascular Adverse Effects Are Still Causing Late Attrition of Novel Therapeutics: Developing Solutions to Detect and Avoid Cardiovascular Toxicity in the Clinic
- Environmental Chemical-Microbiome Interactions in Disease Susceptibility
- Matching Analytical Methods to Markets: Balancing Regulatory Expectations and Technical Challenges **IAT**
- Mechanisms of Ocular Sulfur Mustard Toxicity and Potential Therapies **IAT**
- Reaching Hazard Conclusions for Endocrine-Disrupting Chemicals: Adapting Systematic Review Methods
- Reducing the Uncertainty of Read-Across Predictions by New Approach Methodologies: Application in Regulatory Human Risk Assessments

PLATFORM SESSIONS

- Animal Models
- Autoimmunity/Hypersensitivity/Inflammation
- Zika Pathophysiology and Potential Intervention

9:15 AM to 4:30 PM

POSTER SESSIONS

- Air Pollution: Volatile Organic Compounds
- Alternatives to Mammalian Models II
- Alternatives to Mammalian Models III: Liver, Ocular, and Skin Alternatives
- Animal Models
- Developmental and Juvenile Toxicity
- Education, Outreach, Ethical, and Social Issues
- Metals and Metal Mixtures
- Metals: Mercury and Cadmium
- Modeling of Pharmacokinetics and Biological Effects
- Nanoparticles: Exposure Methods and Safety Regulation
- Nanoparticles: Mechanisms of Toxicity
- Nanoparticles: Protein Biocorona
- Nanotoxicity: Immunology
- Nanotoxicity: *In Vitro*
- Nanotoxicity: *In Vivo*
- Nanotoxicity: Inhalation
- Natural Products
- Neurotoxicology: General
- Non-Pharmaceutical Safety Assessment
- Pharmacokinetics and Disposition
- Respiratory Toxicology: Tobacco Products
- Risk Assessment Applications I
- Risk Assessment Applications II
- Risk Assessment Methods and Policies
- Skin

9:30 AM to 4:30 PM

RESEARCH FUNDING INSIGHTS

- Network with Program Officers

11:00 AM to 12:00 Noon

EUROTOX BO HOLMSTEDT MEMORIAL AWARD LECTURE

- Human Skin Stem Cell-Derived Hepatic Cells and Their Potential Applications in Toxicology
  Lecturer: Vera Rogiers, Vrije Universiteit Brussel

11:00 AM to 12:20 PM

ROUNDTABLE SESSIONS

- Is a Common Mechanism of Action Essential to Conduct a Cumulative Risk Assessment or Just Nice to Have?
- Unlocking the 'Omics Archive: Enabling Toxicogenomic/Proteomic Investigation from Archival Samples

INFORMATIONAL SESSION

- Good Cell and *In Vitro* Method Practices against the "Reproducibility Crisis"

EDUCATION-CAREER DEVELOPMENT SESSION

- Career Opportunities in Regulatory Toxicology

12:30 PM to 1:30 PM

KEYNOTE MEDICAL RESEARCH COUNCIL (MRC) LECTURE

- Circadian Clocks: Setting the Tempo of Our Life
  Lecturer: Michael Hastings, MRC Laboratory of Molecular Biology

1:30 PM to 4:15 PM

SYMPOSIUM SESSIONS

- Atherosclerosis as a Model to Understand the Combined Effects of Environmental Chemical and Non-Chemical Stressors
- Mechanisms of Autophagic Function and Dysfunction in Neurotoxicity and Neurodegeneration
- The Role of the Epigenome in the Etiology of Metal-Induced Disease

WORKSHOP SESSION

- Microbiota as a Target or Mediator of Adverse Effects: Implications for Toxicology

REGIONAL INTEREST SESSION

- Toxicology and Public Health Solutions for Environmental Emergency-Related Contamination Events

PLATFORM SESSIONS

- Alternative Models for Assessing Developmental Toxicity
- Ecotoxicology
- Male Reproductive Toxicity: Evaluating Key Events and Adverse Outcomes
- Pharmacokinetic Modeling: Development and Applications

4:30 PM to 5:50 PM

ROUNDTABLE SESSION

- The Kinetically-Derived Maximum Dose (KMD), a New Dimension to the Maximum Tolerated Dose (MTD)

INFORMATIONAL SESSION

- The US Tox21 Collaboration: A Decade of Experience and a New Vision for the Future

EDUCATION-CAREER DEVELOPMENT SESSION

- Research-Based Approaches to Improve Teaching Effectiveness in Toxicology Classrooms

Thursday, March 15

8:30 AM to 11:15 AM

SYMPOSIUM SESSION

- *In Vitro* Test Methods to Model Local Respiratory Effects after Exposure to Pulmonary Toxicants: Not Just Smoke and Mirrors

WORKSHOP SESSIONS

- A Search for Biomarkers of Neurotoxicity: A Practical Approach
- Deliberations in Regulatory and Safety Assessment of Food Substances in Early Life
- Nonclinical to Clinical Translation of Antibody-Drug Conjugates

INFORMATIONAL SESSION

- The NIEHS Nanotechnology Health Implications Research (NHIR) Consortium

LATE-BREAKING POSTER SESSION

See page 119 for submission information.

SOT | Society of Toxicology
ENDOWMENT
Investing in the Future ...

invest in the future of toxicology

Contributors to the SOT Endowment Fund are helping to build for the future of toxicology through long-term financial support that generates critical resources to enable the Society to fulfill its mission, now and in the years to come. Please help SOT continue to make a difference by becoming a contributor to the SOT Endowment Fund.

Contribute Today!

Visit www.toxicology.org/endowment.

GLOBAL PARTNERS

The Society of Toxicology has established a special category for private, public, and not-for-profit organizations that wish to contribute to the success of SOT toward "creating a safer and healthier world by advancing the science and increasing the impact of toxicology." These organizations provide support for activities aligned with the prediction and prevention of toxicity and disease.

AbbVie, Inc.
North Chicago, Illinois

AstraZeneca
Cambridge, United Kingdom

Bristol-Myers Squibb Company
Pennington, New Jersey

Celgene Corporation
Summit, New Jersey

Chevron Corporation
San Ramon, California

The Coca-Cola Company
Atlanta, Georgia

The Colgate-Palmolive Company
Piscataway, New Jersey

Covance, Inc.
Madison, Wisconsin

The DuPont Haskell Global Centers for Health and Environmental Sciences
Newark, Delaware

Eli Lilly & Company
Indianapolis, Indiana

Envigo CRS Ltd
Huntingdon Cambridgeshire, United Kingdom

ExxonMobil Biomedical Sciences, Inc.
Annandale, New Jersey

Genentech, Inc.
South San Francisco, California

Gilead Sciences, Inc.
Foster City, California

Novartis
Hanover, New Jersey

Oxford University Press
Oxford, United Kingdom

Pfizer, Inc.
Groton, Connecticut

Procter & Gamble Company
Cincinnati, Ohio

Regeneron Pharmaceuticals, Inc.
Tarrytown, New York

Risk Science Center University of Cincinnati College of Medicine
Cincinnati, Ohio

Sanofi
Bridgewater, New Jersey

Syngenta Crop Protection, Inc.
Greensboro, North Carolina

Takeda Pharmaceutical Company Limited
Cambridge, Massachusetts

Western Slope Laboratory, LLC
Troy, Michigan

If your organization is interested in participating in the SOT Global Partner program, please contact Marcia Lawson at marcia@toxicology.org.

Attend the Meeting

Reasons to Attend

Beyond being the largest meeting and exhibition dedicated to toxicology in the world with more than 6,500 toxicologists and 330 exhibitors anticipated, there are plenty of compelling reasons to join SOT for its 57th Annual Meeting and ToxExpo.

Innovative Science

From basic and applied research to cutting-edge topics, more than 170 Scientific Sessions and 2,500 presentations will be featured, making this meeting *the* event to learn about all the advances in toxicology that have taken place during the last year.

Global Networking

Attendees have hundreds of opportunities to connect with leading scientists from around the world through the Scientific Sessions, ToxExpo, receptions, and other meeting activities. More than 20% of attendees come from outside North America, representing more than 50 countries.

Partnership Opportunities

The ToxExpo Exhibit Hall features 300+ exhibiting companies who provide attendees with the opportunity to interact with the newest equipment and proven technology providers. See pages 120–123 for more details on ToxExpo.

Affordability and Value

The meeting is cost effective, providing attendees with five days of sessions and events featuring the latest scientific insights and discoveries. SOT members, postdoctoral researchers, and graduate students receive special discounts on registration, and SOT arranges for exclusive airfare discounts and hotel rates for meeting attendees.

Culture and History

The Henry B. González Convention Center and SOT hotels are just steps from historic and cultural landmarks, such as the Alamo and River Walk, some of which date to the early 1700s. With temperatures expected to be in the 70s Fahrenheit (low 20s Celsius), San Antonio is yours to explore.

Discover San Antonio

San Antonio restaurants and businesses participate in a meeting badge discount program.

Visit www.visitsantonio.com/2018-sot for information on this program and San Antonio.

Accessibility for Persons with Disabilities

The Henry B. González Convention Center and most of the SOT hotels are accessible to persons with disabilities. If you require special services, please let SOT know by indicating your needs while registering or by contacting Heidi Prange by email heidi@toxicology.org or call 703.438.3115.

To arrange special services, SOT recommends the following two providers for language and mobility needs.

LSA Interpretation Services

800.305.9673 | www.lsaweb.com

Language Services Associates (LSA) is a nationwide, full-service firm providing translators and interpreters in 180 languages.

Scootaround

888.441.7575 | www.scootaround.com

Scootaround is a leading source for wheelchair, scooter, and power-chair rentals.

Attire

Business casual. No coat or tie required! Bring comfortable clothing and shoes for walking the large conference center. Dress in layers, as meeting rooms sometimes fluctuate in temperature.

Badges and Event Tickets

If you register by January 12, 2018, you will receive your badge, event tickets, and other requested registration materials in the mail. Please remember to bring these items with you to San Antonio, as your badge is your admission to the meeting, sessions, and events. Tickets for CE courses and other events also may be required and are issued with your meeting badge.

If you register after January 12, 2018—or did not receive your badge or misplaced it—go to the "BADGE PICK UP" registration counters on-site to pick up your badge. You will be asked to show a photo ID.

Badge holders and the printed *Program* will be available on-site near registration. If you ordered a printed copy of *The Toxicologist*, it can be acquired at a special registration counter.

If you have not registered for the meeting before you arrive in San Antonio, please complete the on-site registration form found at the kiosks in the registration area and proceed to the appropriate registration line.

Additional registration information is available starting on page 22.

Safety and Security

San Antonio is a safe and vibrant city that has amazing culture and natural beauty. As with all SOT Annual Meeting and ToxExpo locations, meeting attendees are encouraged to walk "smart" when you leave the Henry B. González Convention Center:

- Know your destination and the best way to reach it.
- Travel along sidewalks in lighted areas at night and don't walk alone.
- Establish a "buddy" system with another meeting attendee.
- Share schedules and check on each other periodically.
- Build your awareness of unknown surroundings by reviewing local information.
- Laptop computers are attractive, easy targets for thieves. Be sure your laptop is in a secure place.
- Jackets with pockets provide a convenient alternative for women to reduce the chance for lost or stolen handbags.

CENTRO San Antonio Ambassadors can be quickly spotted in yellow uniforms and straw hats across downtown San Antonio. They are always willing to help tourists and locals alike with anything from directions to historical facts and details on special events. They are equipped with two-way radios and qualified to provide first-aid assistance.

Visa Information

Tips for applying for a visa:

- **Start Early**—The US is advising visa applicants to apply at least three to four months in advance of their travel date. Also, additional reviews may be required. This could add an additional four to six weeks to the processing time.
- **Gathering Your Application Materials**—Organize your passport; necessary applications; supporting documents, including information on employment, reason for travel, and financial status; and proof of payment of fees. For more detailed information on visa requirements, consult the US Department of State's visa site and the International Visitors Office of The National Academies.
- **Submitting Your Application**—Make an appointment to visit your US Embassy or Consulate. Make sure you ask if there are any fees required. Most fees must be paid before your appointment. Wait times for appointments may be longer than in the past. Schedule the appointment as soon as possible. Information on visa wait times can be found at the US Department of State website.

If you need additional visa assistance, contact the International Visitors Office of The National Academies (www.nationalacademies.org/visas).

If you need a formal invitation letter for visa purposes, you may request an invitation by sending your name, address, and other contact information to the SOT Registration Department by email sotmeetings@toxicology.org or call 703.438.3115. If you have been accepted to make a presentation at the meeting, please include the name and date of your presentation. You will need to make your own hotel reservations and register for the meeting.

Hotel and Travel

Housing

The Society of Toxicology has reserved and arranged for discounted room rates at various San Antonio hotels—known as the SOT hotel room block. Booking a room in the room block is an important way to support the Society and keep overall meeting costs as low as possible. By booking a room in the SOT hotel room block through SOT's official housing partner Connections Housing, you get exclusive hotel rates, increase your networking opportunities by staying in the same locations as other attendees and exhibitors, and receive full-service assistance in finding the perfect room, securing it, and making updates to your reservation without any pre-payment required.

Hotel Reservation Information

All reservations for housing must be made through Connections Housing and not with the hotels directly. The deadline date for housing reservations is February 21, 2018. Please choose only one of the following methods to make your reservation. For best availability and immediate confirmation, make your hotel reservation via internet or by telephone. Faxed and mailed housing requests will take longer to process and your hotel selections may not be available.

- **www.toxicology.org/housing**
- **Mail Housing Form to:**
  Connections Housing
  950 Scales Road, Building 200
  Suwanee, GA 30024 United States
- **Tel:** 800.262.9974 (USA) or 404.842.0000
  (USA and outside the USA)
- **Fax:** 678.228.1920
  (USA and outside the USA)
- **Hours of Operation:**
  8:30 AM–7:00 PM (ET) Monday–Friday

Hotel Acknowledgment

A reservation acknowledgment will be emailed, faxed, or mailed via Connections Housing to you once your reservation has been booked. (You will not receive a confirmation from your hotel.) If you do not receive an acknowledgment within three business days, please call Connections Housing.

Changes and Cancellations

You can make changes and/or cancellations online or by contacting Connections Housing at 404.842.0000 or 800.262.9974. All cancellations made within 72 hours prior to the day of arrival and no shows will be charged the first night's room and tax by the hotel. Early departures are subject to penalty fees set by the hotel.

Room-Share Program

The Society is pleased to provide a Room-Share Program to those registered for the Annual Meeting. It is available to each meeting registrant who voluntarily enrolls in the program and accepts the terms of the legal disclaimer. This program allows SOT Annual Meeting registrants to identify others with whom a room might be shared. For more information on this program and to sign up, visit the SOT Annual Meeting website.

Transportation

Air Transportation

San Antonio is serviced by San Antonio International Airport (SAT), which is a 15-minute drive from the Henry B. González Convention Center and the SOT hotel area. The airport offers flights visiting over 30 nonstop domestic and international destinations on 10 different carriers. For more information, visit www.sanantonio.gov/sat.

Preferred Carrier Airfare Discounts

SOT has established discounted rates through United and Delta Airlines on select routes to San Antonio. Be sure to use the appropriate reference numbers when making your reservation. You may purchase your ticket online, call the airline directly using the toll-free numbers, or provide your travel agent with the reference/discount numbers listed below to receive the discount.

Delta Airlines

Tel: 800.328.1111 | www.delta.com/meetings
SOT Discount Code: NMR8X

Use offer code **NMR8X** to receive a discount up to 10%. Discount is valid for travel March 6, 2018, through March 18, 2018.

Attendees coming from outside the US should call their local Delta Airlines reservations office or email deltameetingnetwork@delta.com with their preferred itinerary and discount codes.

United Airlines

Tel: 800.426.1122 *(a service fee will apply)* **| www.united.com** *(no service fees)*
SOT Discount Code: ZEET346392

Use offer code **ZEET346392** to receive a discount up to 10%. Discount is valid for travel March 6, 2018, through March 18, 2018.

Attendees coming from outside the US should call their local United Airlines reservations office or email groupmeetings@united.com with their preferred itinerary and discount codes.

If you are booking through a travel professional, please give them the following information to receive a discount: **Agreement Code: 346392, Z Code: ZEET**.

SOT Air Travel Provider—ATC Travel Management

ATC Travel is the official travel management firm for the SOT 57th Annual Meeting and ToxExpo.

Tel: 800.458.9383 | www.atcmeetings.com/sot
Email: reservations@atcmeetings.com
Hours of Operation: 8:30 AM–7:00 PM (ET) Monday–Friday

Please note that depending on your reservation method, ATC Travel Management charges a $10 online service fee or a live-agent reservation fee.

To obtain the maximum discounted fares, call at least 60 days prior to departure and identify yourself as a Society of Toxicology meeting attendee. ATC Travel Management will find the best fare for you and email you an itinerary.

(continued on page 21)

Hotel Map

1	Grand Hyatt San Antonio *(SOT Headquarters Hotel)*	7	Hyatt Regency San Antonio Riverwalk
2	Courtyard San Antonio Riverwalk	8	La Quinta Inn & Suites San Antonio Riverwalk
3	Hilton Palacio del Rio	9	Marriott Rivercenter San Antonio
4	Holiday Inn	10	Marriott Riverwalk San Antonio
5	Hotel Indigo at the Alamo	11	Omni La Mansión del Rio
6	Hotel Valencia Riverwalk	12	Residence Inn by Marriott
	Henry B. González Convention Center	13	Westin Riverwalk San Antonio

Hotel Services

Hotel	Rewards Program	Blocks to Convention Center	Single/Double Rate	Restaurant	Complimentary Breakfast	In-Room Safe	Complimentary Fitness Center	Swimming Pool	Business Center	Complimentary In-Room Internet	Room Service	Gift Shop	Overnight Self Parking**	Valet Parking Per Night**	AAA Rating
1) **Grand Hyatt San Antonio** *(SOT Headquarter Hotel)* 600 East Market Street	World of Hyatt	Adjacent	$235	✓		✓	✓	✓	✓	✓	✓	✓	$29	$39	4 Stars
2) **Courtyard San Antonio Riverwalk** 207 North Saint Mary's Street	Marriott Rewards	7 Blocks	$199	✓			✓	✓	✓	✓				$31	4 Stars
3) **Hilton Palacio del Rio** 200 South Alamo Street	Hilton Honors	1 Block	$235	✓		✓	✓	✓	✓	✓	✓	✓	$29	$42	4 Stars
4) **Holiday Inn** 217 North Saint Mary's Street	IHG Rewards	7 Blocks	$235	✓		✓	✓	✓	✓	✓	✓		$25	$30	4 Stars
5) **Hotel Indigo at the Alamo** 105 North Alamo Street	IHG Rewards	5 Blocks	$179	✓			✓		✓	✓	✓			$27	4 Stars
6) **Hotel Valencia Riverwalk** 150 East Houston Street	V-VIP Program	6 Blocks	$229	✓	✓	✓	✓			✓	✓			$34	4 Stars
7) **Hyatt Regency San Antonio Riverwalk** 123 Losoya Street	World of Hyatt	4 Blocks	$199	✓		✓	✓	✓	✓	✓	✓		$31	$43	4 Stars
8) **La Quinta Inn & Suites San Antonio Riverwalk** 303 Blum Street	La Quinta Returns	1 Block	$199		✓		✓	✓	✓	✓		✓	$25	$30	3 Stars
9) **Marriott Rivercenter San Antonio** 101 East Bowie Street	Marriott Rewards	1 Block	$239	B/L*		✓	✓	✓	UPS Store	✓	✓	✓	$37	$42	4 Stars
10) **Marriott Riverwalk San Antonio** 889 East Market Street	Marriott Rewards	Across Street	$239	B/L*		✓	✓	✓	✓	✓	✓	✓		$42	4 Stars
11) **Omni La Mansion del Rio** 112 College Street	Select Guests	5 Blocks	$235	✓		✓	✓	✓	✓	✓	✓			$40	4 Stars
12) **Residence Inn by Marriott** 425 Bonham Street	Marriott Rewards	4 Blocks	$199		✓	✓	✓	✓		✓			$28	$28	4 Stars
13) **Westin Riverwalk San Antonio** 420 West Market Street	Starwood Program	3 Blocks	$235 *(City Side)* $255 *(River Side)*	✓		✓	✓	✓	✓	✓	✓	✓		$39	4 Stars

*Breakfast/Lunch Only | **Rates Subject to Change

All hotel accommodations, rates, internet access, and parking pricing are subject to change. Early departures are subject to penalty fees set by the hotels. Although making your reservations outside of the SOT hotel block can sometimes be more economical, it decreases the money available to the Society to carry out its strategic goals and may cause the Society to pay attrition fees for unutilized hotel rooms. In addition, the Society is unable to assist you if you have any difficulties with your room reservation, such as the hotel over-booking or misplacing your reservation. SOT depends on the Annual Meeting revenue (hotel room commissions and rebates) to fund other programs throughout the year and to keep future registration fees low. Please assist the Society by making your hotel room reservation through SOT Housing Bureau. Rates shown are for single and double occupancy; additional fees may apply for additional guests. Please note: services offered, taxes, and fees associated with hotel services are subject to change and availability, tax rate 14.75%. Information listed is complete and accurate as of July 1, 2017.
Note: Checkout times usually are between 11:00 am–1:00 pm; Check-in times usually are between 2:00 pm–4:00 pm.

SOT | Society of Toxicology

Become an SOT Member

Special Offer for Nonmember 2018 Annual Meeting Attendees:

Submit your completed application for the March review cycle (deadline March 31, 2018) and, upon acceptance, SOT will waive your 2018 membership dues.

Member Benefits Include:

- Discounted registration rates for SOT-hosted meetings.
- Ability to communicate and collaborate with colleagues from industry, government, and academia.
- Access to *Toxicological Sciences*, the official journal of the Society.
- Connections to Regional Chapters, Special Interest Groups, and Specialty Sections.
- Qualification for more than 45 SOT Awards.
- Career and education resources.

Choose the membership level that's right for you:

Full • *Associate* • *Postdoctoral* • *Graduate Student*

Reduced dues available to members from developing countries.

8,200 members from more than 70 countries

Join the SOT community by completing the online membership application at www.toxicology.org.

(continued from page 17)

Before contacting ATC Travel Management, please gather the following information:

- Your name as it appears on your ID and your date of birth
- The desired dates of arrival to and departure from San Antonio
- Your home city or originating airport
- Your approximate time of departure from the originating airport
- The number of persons traveling (adults/children)
- Your method of payment, either credit card or check
- Your airline frequent flyer number(s)

Ground Transportation from the Airport

Ground transportation is located curbside outside the baggage claim area in Terminals A and B. For assistance, contact an airport ground transportation employee, who can be identified by the uniform red shirts.

Car Rental

Arriving passengers can use the courtesy phones provided at the car rental counters located in Terminal A to request shuttle transport to the car rental company of their choice after hours or can proceed to the shuttle pick-up area located outside the baggage claim area. Rental car facilities are located near the airport. Contact information for the car rental agencies that service the airport can be found on the San Antonio International Airport website.

Public Transportation

VIA Metropolitan Transit is San Antonio's public transportation agency. VIA's airport bus stop is located on the far west end of Terminal B. You will catch VIA bus route five, which operates everyday and arrives in downtown San Antonio in about 30 minutes; the fare will be $1.30.

Shuttle Services

SuperShuttle and Execucar provide service between SAT Airport and major hotels in the downtown area. Shuttle service is operated 24/7 daily. Book online and receive an additional discount of 10% off service by using the following link: group.supershuttle.com/group-page/sottransportation.

For more information, visit www.supershuttle.com or call 1.800.258.3826.

Taxi

Fares to downtown San Antonio start at $29. More details on fees and contact information for taxicab companies that service the airport are available on the San Antonio International Airport website. Uber and Lyft services also are available in San Antonio.

San Antonio in March…
76°F to 51°F

For an up-to-date, detailed weather forecast, visit the National Weather Service Forecast Office at www.weather.gov/ewx.

Train Transportation

AMTRAK

Tel: 800.872.7245 | www.amtrak.com

Amtrak operates out of San Antonio Station, which is a three-minute drive from the Henry B. González Convention Center and the SOT hotel area. There are always taxis ready and waiting outside the station.

Ride-Share Program

SOT is offering a Ride-Share Program in conjunction with the Annual Meeting and ToxExpo for those who wish to reduce travel expenses. Once you have registered for the Annual Meeting, visit the SOT Annual Meeting website to enroll in the Ride-Share Program, view other enrollees, and make transportation arrangements.

Getting around Town

Public Transportation

For information regarding VIA Metropolitan Transit's Day Pass and downtown streetcar service, visit the VIA website www.viainfo.net or call 1.866.362.2020.

Henry B. González Convention Center Location and Parking

Henry B. González Convention Center
900 E. Market Street
San Antonio, Texas 78205

Ample public parking is available in close proximity to the convention center for an hourly/daily fee. Check the Henry B. González Convention Center website for more information about parking.

Please review the SOT Hotel Services chart on page 19 for valet and self-parking rates for your hotel.

Registration

Registration Deadlines

Registration for the Annual Meeting is open now. Register by January 12 to obtain the early-bird rate and to ensure that you receive your registration materials before the meeting. You can register online, via fax, or by mail to SOT Headquarters.

- Early-Bird Registration: **January 12, 2018**
- Standard Registration: **February 9, 2018**
- Final Registration: **After February 9, 2018**

How to Register

Online Registration

SOT members and nonmembers are invited to register for the 2018 SOT Annual Meeting using the SOT Online Registration System. The system is designed for those who will be paying the registration fee by credit card. Registration can be accessed via the SOT website at www.toxicology.org/register.

The online registration system will be open throughout the meeting, and if you register online after March 8, 2018, you can easily pick up your badge at the "BADGE PICK UP" registration counters.

Confirmation

Online registrants will receive an electronic confirmation following registration. If you do not, please send an email to sotmeetings@toxicology.org. All registrants will be mailed a registration confirmation, name badge, and Continuing Education and/or event ticket(s) before the meeting if the registration form is received by January 12, 2018. If your registration is received after January 12, you can pick up your badge and tickets at the "BADGE PICK UP" registration counters on-site. You do not need to enter the regular registration line.

Mail or Fax Registration

Registrants may fax or mail their registration payments using the registration form located on pages 24–25. No phone registrations will be accepted.

Please send registration forms to:

SOT Headquarters
11190 Sunrise Valley Drive, Suite 300
Reston, VA 20191

Fax: 703.438.3113 *(Faxes require credit card payment)*

Forms will be date-stamped as they arrive. This is your date of registration. Fax registrations will be accepted by SOT Headquarters only if a credit card number is clearly listed in the appropriate area. SOT needs only one copy for processing.

DO NOT mail your registration form to SOT if it will arrive after March 8, 2018. SOT will accept Annual Meeting registrations until March 8. After March 8, registrations not processed online will only be accepted on-site at the Annual Meeting.

Payment

Registration forms must be accompanied by one of the following methods of payment:

- Check (company or personal), United States currency only. Please list all registrants on check memo or check stub.
- Government Purchase Order (Check must be drawn from the US Department of Treasury.)
- Money Order
- Visa, MasterCard, Discover, Diner's Club, or American Express

Exhibitor Registration

To register exhibitor booth staff, please visit www.ToxExpo.com and log into the Exhibitor Service Center using your company password, which was provided in your booth confirmation email. For more information, please email sot_exhibits@toxicology.org.

Guest/Spouse Registration

If a non-scientist is accompanying you to the meeting, guest registration is available. You may register your guest while registering for the meeting. If you have already registered for the meeting, complete the Registration Form, marking the appropriate sections for guest registration and send it to SOT Headquarters along with a copy of your registration confirmation.

The SOT Guest/Spouse Hospitality Room, located at the Grand Hyatt, provides guest registrants with a place to meet and socialize. The room will be open Sunday through Thursday.

Reminder: Guest registrants and children under age 15 are not permitted in the ToxExpo Exhibit Hall at any time or in Scientific Sessions. Only the Scientific Session Chairs can give permission for attendance for sessions held outside the Exhibit Hall. Please contact David Rosse to inquire about obtaining permission in advance.

Cancellation Refund Policy

All requests for cancellations and/or refunds must be received in writing at SOT Headquarters by February 9, 2018. These refunds will be processed, less a $50 cancellation fee, following the Annual Meeting. Refund requests received after February 9, 2018, will not be processed.

Attend the SOT Contemporary Concepts in Toxicology (CCT) Meetings

Two CCT meetings will be held in San Antonio on Saturday, March 10, prior to the start of the SOT Annual Meeting and ToxExpo.
See page 55 for details.

Attendee Registration Form

SOT 57th Annual Meeting • March 11–15, 2018

R2018

FOR OFFICE USE ONLY
Date Received: _____
Input: ❑ Initials: _____

PLEASE PRINT CLEARLY OR TYPE
(**Required:** Please check the appropriate box)

❑ SOT Member ❑ Nonmember Badge Name: _____

First Name/Middle Initial: _____

Last Name: _____ Professional Degree(s): _____

Organization/University: _____
(Is this a new employer and/or new address? _____ Yes _____ No)

Company (second line): _____

Department: _____

Street Address: _____

City/Region: _____ State/Prov: _____ Postal Code: _____ Country: _____

Area Code/Telephone Number: _____ Fax Number: _____

Email Address: _____

Special Accessibility Requirements: _____

If you are a Student or Postdoc registrant, please complete the following information:

❑ Postdoc ❑ Graduate Student ❑ Undergraduate Student (Fax or mail a copy of Student ID with the form)

Institution: _____ Advisor's Name: _____

Advisor's Telephone Number: _____ Advisor's Email: _____

REGISTRATION FEES:

❑ I'm Already Registered	Early-Bird Registration (Received by Jan. 12)	Standard Registration (Jan. 13 to Feb. 9)	Final Registration (After Feb. 9*)	
SOT Member	$340	$400	$460	$ _____
Nonmember**	$700	$760	$820	$ _____
SOT Retired/Emeritus Member	$ 70	$120	$170	$ _____
SOT Postdoctoral Member	$ 85	$135	$185	$ _____
Postdoctoral Nonmember**	$170	$220	$270	$ _____
SOT Graduate Student Member	$ 65	$115	$165	$ _____
Graduate Student Nonmember**	$130	$180	$230	$ _____
Undergraduate Student *(Copy of Student ID Required)*	$ 0	$ 0	$ 0	$ _____
High School Student *(Copy of Student ID Required)*	$ 0	$ 0	$ 0	$ _____
SOT Global Partner *(One Complimentary Registration per Company)*	$ 0	$ 0	$ 0	$ _____
Press	$ 0	$ 0	$ 0	$ _____
Guest/Spouse *(Nonscientist/No access to the Scientific Sessions or ToxExpo)*	$ 70	$ 85	$100	$ _____

Guest/Spouse Name: _____

METHOD OF PAYMENT:

All registrations submitted by hard copy or fax will be processed online by SOT staff.

❑ Check or Money Order # _____
(PAYABLE TO "SOCIETY OF TOXICOLOGY")

❑ Government Purchase Order # _____
(US GOVERNMENT PO FORM MUST BE ATTACHED)

❑ American Express ❑ Diner's Club ❑ Discover ❑ MasterCard ❑ Visa

Registration Fee(s) (from page 1) $ _____

Continuing Education Courses (from page 2) $ _____

Student and Postdoc Functions (from page 2) $ _____

Printed Materials (from page 2) $ _____

TOTAL DUE $ _____

Credit Card #: _____ Expiration Date: _____

Signature: Cardholder's Printed Name:

By registering for the SOT Annual Meeting you agree to the terms and conditions outlined in the registration policies on page 26.

* After February 9, final registration rates apply. SOT will accept faxed registration forms until March 8. Online registration will be open until March 15. On-Site registration forms will be available at the Annual Meeting Registration Desk.

** Special offer to nonmember 2018 Annual Meeting attendees: Submit your completed application for the March review cycle (deadline March 31, 2018) and, upon acceptance, SOT will waive your 2018 membership dues.

RETURN THIS TWO-PAGE FORM WITH PAYMENT TO:
SOT Headquarters Registration Dept., 11190 Sunrise Valley Drive, Suite 300, Reston, VA 20191-4375

Faxed forms are accepted only if using a credit card. Fax form to: 703.438.3113.
US GOVERNMENT PURCHASE ORDERS MUST BE FAXED OR MAILED WITH THE REGISTRATION FORM.
***Questions?* Contact SOT • Tel: 703.438.3115 • Email: sothq@toxicology.org**

(***Part 2*** *continued on next page)*

Attendee Registration Form *(Part 2 continued from previous page)*

SOT 57th Annual Meeting • March 11–15, 2018

CONTINUING EDUCATION COURSES:

❑ **Yes, I would like to attend the following CE courses. (Only meeting registrants may enroll in a CE course.)** *(Only 1 per time slot)* **AM #**_____ **PM #**_____

Visit www.toxicology.org/sot-ce to view course list and numbers.

	Early-Bird Registration (Received by Jan. 12)	Standard Registration (Jan. 13 to Feb. 9)	Final Registration (After Feb. 9)	# of Courses	
SOT Member/Global Partner	$150 each	$185 each	$220 each	x_____	$_____
SOT Retired/Emeritus Member	$110 each	$145 each	$180 each	x_____	$_____
Nonmember	$300 each	$335 each	$370 each	x_____	$_____
Postdoctoral (SOT Member/Nonmember)	$ 90 each	$125 each	$160 each	x_____	$_____
Graduate or Undergraduate Student (SOT Member/Nonmember)	$ 45 each	$ 80 each	$115 each	x_____	$_____
Press	$ 0	$ 0	$ 0	x_____	$_____

Yes, I would like to attend a Sunrise CE Mini-Course (includes continental breakfast). *(Pick one)* ❑ **SR01** ❑ **SR02**

SOT Member/Global Partner	$ 55	$ 90	$125	$_____
SOT Retired/Emeritus Member	$ 55	$ 90	$125	$_____
Nonmember	$ 75	$110	$145	$_____
Postdoctoral (SOT Member/Nonmember)	$ 55	$ 90	$125	$_____
Graduate or Undergraduate Student (SOT Member/Nonmember)	$ 25	$ 60	$ 95	$_____
Press	$ 0	$ 0	$ 0	$_____

STUDENT AND POSTDOCTORAL FUNCTIONS:

❑ **Yes, I am an undergraduate student and would like to attend the Sunday Undergraduate Education *Program*.** *(Limited seating and ticket required)* $ Complimentary

❑ **Yes, I am a student or postdoctoral registrant and would like to attend the complimentary Student/Postdoctoral Mixer on Sunday, 7:30 pm–9:00 pm.** *(Ticket required)* $ Complimentary

❑ **Yes, I would like to attend the Mentoring Breakfast on Monday, 6:15 am–7:45 am, as a mentee.** *(Limited seating and ticket required)* $ 10

Yes, I am a graduate student or postdoctoral member registrant and would like to attend a complimentary Trainee Discussion.

Select one only: *(Limited seating and ticket required)*

❑ **Monday, 9:45 am–10:45 am, Trainee Discussion with Plenary Speaker** $ Complimentary

❑ **Wednesday, 2:00 pm–3:00 pm, Trainee Discussion with Medical Research Council (MRC) Lecturer** $ Complimentary

❑ **Yes, I am a student or postdoctoral registrant and would like to attend the *In Vitro* Lecture and Luncheon on Monday, 11:30 am–1:00 pm.** *(Ticket required)* $ 10

❑ **Yes, I am a postdoctoral registrant and would like to attend the Postdoctoral Luncheon on Tuesday, 12:20 pm–1:20 pm.** *(Limited seating and ticket required)* $ 10

❑ **Yes, I am a student or postdoctoral registrant and would like to attend Career Exploration Session on Tuesday, 1:25 pm–2:45 pm.** *(Limited seating and ticket required)* $ Complimentary

PRINT MATERIALS:

In an effort to conserve resources, the printed *Program* will be mailed ONLY by request (in the US and Canada only). If you wish to receive your printed *Program* before the meeting, please mark this checkbox and it will be mailed to you in early March (in the US and Canada only). The *Program* will be available for download via the SOT website in January and for pick up on-site.

❑ **Yes, I want to receive the printed *Program* in the mail** (option not available after February 9, 2018). $ 20

2018 Annual Meeting registrant fees include access to the abstracts as a downloadable PDF of *The Toxicologist* via the SOT website.

❑ **Yes, I want to purchase the printed version of *The Toxicologist*** (available for pick up on-site while supplies last). **$50** each x_____ $_____

REGISTRANT—CIRCLE ALL THAT APPLY: (YOU MUST MAKE ONE SELECTION/CATEGORY)

A. Type of Organization:
1. Academia
2. Consultant
3. Contract Research
4. Government
5. Military
6. Private Industry
7. Other _____

B. Job Function:
8. Analytical
9. Financial/Purch.
10. Computer/Statistics
11. Health and Safety
12. Mgmt. Corporate
13. Mgmt. Facilities
14. Mgmt. Personnel
15. Marketing/Sales
16. Quality Assurance
17. Regulatory
18. R&D Admin.
19. R&D Operations
20. R&D Technical
21. Teaching
22. Other_____

C. Field of Work:
23. Biological Modeling
24. Biotechnology
25. Carcinogenesis
26. Cardiovascular
27. Clinical & Transl. Tox.
28. Comparative and Vet.
29. Computational Tox.
30. Dermal Tox.
31. Drug Discovery Tox.
32. Epidemiology
33. Ethical, Legal, Forensics, and Societal Issues
34. Exposure
35. Food Safety
36. General Tox.
37. Genetic Tox.
38. Immunotoxicology
39. Infusion Tox.
40. Inhalation Tox.
41. *In Vitro* and Alt. Methods
42. Mechanisms
43. Medical Devices
44. Metals
45. Methods
46. Mixtures
47. Molecular Biology
48. Mutagenicity
49. Nanotoxicology
50. Neurotoxicology
51. Occup. and Public Health
52. Ocular Tox.
53. Pathology
54. Pharmacokinetics
55. Pharmacology
56. Risk Assessment
57. Reg. and Safety Eval.
58. Repro. and Develop. Tox.
59. Stem Cells
60. Other _____

D. Product Interest:
61. Publications
62. Contract Services:
    a. Analytical
    b. Aquatic Tox.
    c. Clinical Tox.
    d. Computer
    e. *In Vitro* Tox.
    f. Metabolic Profile
    g. Pathology
    h. Preclinical Tox.
    i. Quality Assurance
    j. Wildlife Tox.
63. Supplies/Equipment
    a. Analytical
    b. Clinical Chem.
    c. Hardware
    d. Software
    e. *In Vitro*
    f. *In Vivo*
    g. Lab Animal
    h. Neurotoxicology
    i. Pathology
    j. Radioactive Isotope
64. Other_____

E. Purchasing Responsibilities:
65. a. I make purchasing decisions
    b. I influence purchasing decisions
    c. I do not participate in purchasing decisions

There will be no refunds for cancellations received at SOT Headquarters after February 9, 2018.

SOT will accept faxed registration forms until March 8. Online registration will be open until March 15.
On-Site registration forms will be available at the Annual Meeting Registration Desk.

Registration Materials

Badges

Badges and event tickets will be mailed in advance if you register by January 12, 2018. If you need to register or have not received your badge, assistance will be available on-site in the registration area.

NOTE: If you are registered and have your badge, you do not need to enter the registration line.

Program

The printed *Program* will be mailed ONLY by request (in the US and Canada only). If you wish to receive your printed *Program* before the meeting, please select the appropriate box on the registration form. Submission must occur by February 9. The *Program* will be mailed to you in late February (in the US and Canada only). The *Program* also will be available for download via the SOT website in early February and for pick up on-site. See page 32 for more details about the *Program* and *The Toxicologist*.

The Toxicologist

The Toxicologist contains the abstracts for the meeting. A printed copy of *The Toxicologist* may be purchased by selecting the appropriate box on the registration form. Printed copies will be available on-site in the registration area. A PDF version will be available for download via the SOT website.

Tickets

Tickets are required for Continuing Education (CE) courses and some other events. If you have these events on your registration form, your tickets will be issued with your meeting badge. Annual Meeting registration is required to participate in CE and other activities.

2018 SOT Annual Meeting Policies

By registering for the 2018 SOT Annual Meeting, you are agreeing to the following terms and conditions:

For individuals who are not members of SOT, participation in SOT's Annual Meeting and ToxExpo is available only to bona fide individuals who are engaged in or promote the field of toxicology or biotechnology research and support the growth and development of the toxicology field. For organizations, participation in SOT's Annual Meeting and ToxExpo is available only to bona fide organizations with public policy positions and business practices that are generally consistent with SOT's mission, goals, reputation, and its policies and principles as determined by SOT. SOT reserves the right to review applications for participation at SOT's Annual Meeting and ToxExpo to confirm that the applicant meets these criteria and may, at SOT's sole discretion, reject a registration by any individual or organization or withdraw registration privileges at any time if any individual or organization is found to be inconsistent with SOT's principles and interests.

Unless written notification by the registrant, stating otherwise, is submitted to SOT Headquarters prior to the Annual Meeting or while registering on-site, SOT Annual Meeting registrants grant SOT permission:

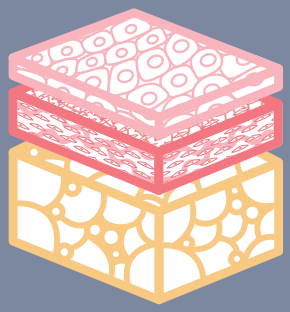
- To reproduce, copy, and publish image, voice, and any or all media taken at the Annual Meeting.
- To share registrant contact information with organizations that SOT believes might have a product or service of interest to you. Limited data provided to third parties include name, affiliation, and business address. Your telephone, fax numbers, and email will not be disclosed to third parties.
- To share registrant name and affiliation with SOT exhibiting companies.
- To be included in the attendee listing accessible to meeting registrants using the SOT Mobile Event App—registrant name and affiliation shared.

SOT Annual Meeting registrants are prohibited from:

- Inviting children under the age of 15 and guest/spouse registrants into the ToxExpo Exhibit Hall. (Session chairs must provide consent for the guest/spouse or child to attend sessions.)
- Soliciting in the ToxExpo Exhibit Hall unless they are a current exhibitor. SOT retains the right to have removed from the exposition any company that has not duly contracted for exhibit space.
- Taking photographs or other electronic capture of Scientific Sessions in meeting rooms or the ToxExpo without the consent of the session chair and the presenter(s)/author(s).
- Photographing colleagues against the backdrop of scientific posters on display without the express consent of the presenting author(s).
- Photographing exhibit booths.
- Speaking on a cell phone while attending Scientific Sessions.

The policies adopted above will be enforced by the Society. Those individuals who do not comply will be asked to leave the session or ToxExpo floor. If you have any questions regarding these policies, please contact the SOT Headquarters Office.

SOT | Contemporary Concepts in Toxicology



Building a Better Epithelium

Breaking the Barrier to the Next Generation of Toxicity Testing

March 10, 2018 | San Antonio, Texas

www.toxicology.org/epithelium

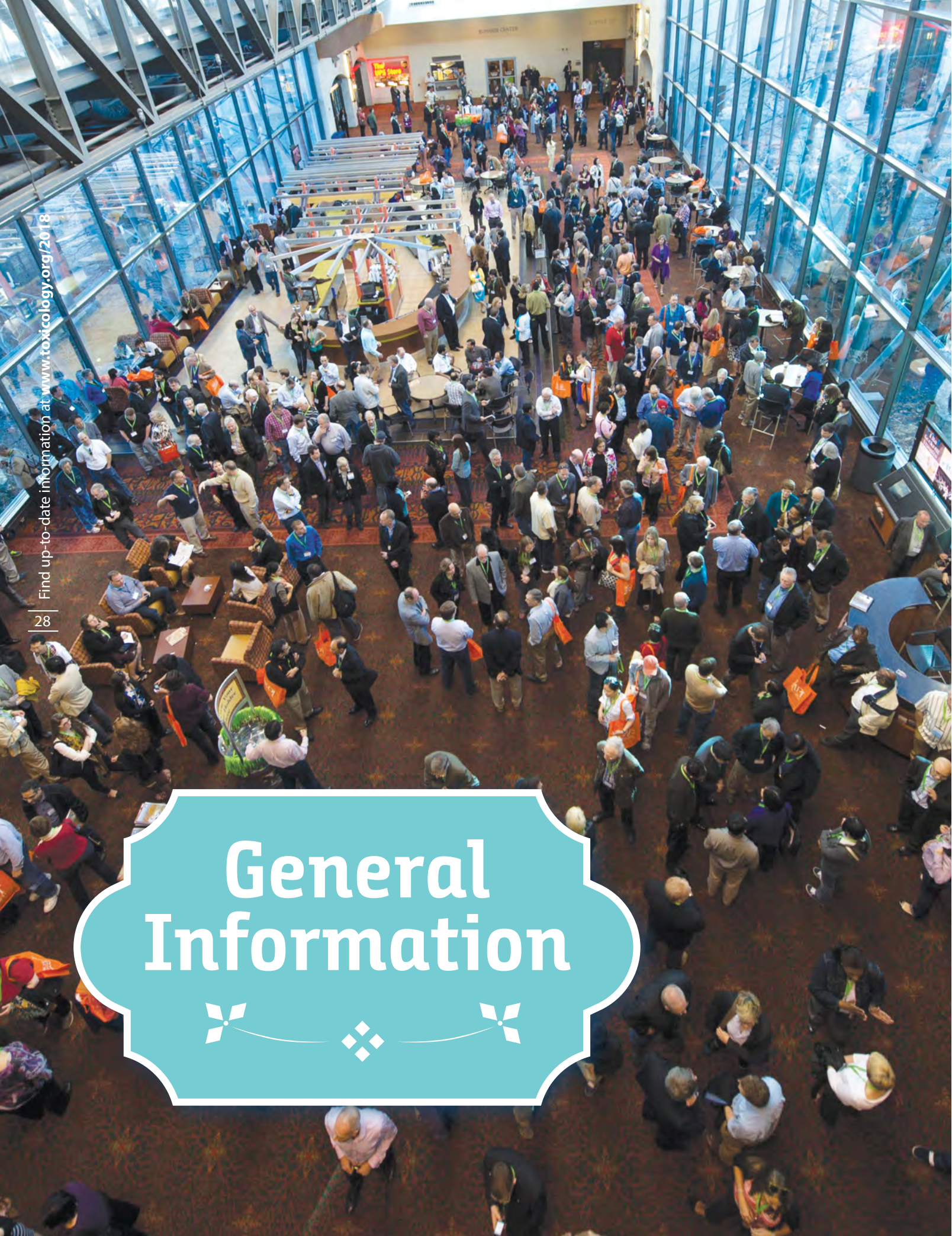
Register for an Upcoming Meeting

Toxicological Concerns in Older Adults

A Neglected Majority

March 10, 2018 | San Antonio, Texas

www.toxicology.org/agingcct



General Information

On-Site Services

SOT Contacts Tel: 703.438.3115

Awards and Fellowships
Raul Suarez | Extension 1461 | raul@toxicology.org

Career Resource and Development
Kimberly von Brook | Extension 1600 | kimberly@toxicology.org

Continuing Education
Kevin Merritt | Extension 1601 | kevin@toxicology.org

Education
Betty Eidemiller | Extension 1430 | bettye@toxicology.org

Exhibits
Tonja Morrow | Extension 1454 | tmorrow@toxicology.org

Global Gallery of Toxicology
Kevin Merritt | Extension 1601 | kevin@toxicology.org

Graduate Students
Ashley Black | Extension 1402 | ashley@toxicology.org

Marketing and Advertising Opportunities
Tonja Morrow | Extension 1454 | tmorrow@toxicology.org

Media
Michelle Werts | Extension 1640 | michelle@toxicology.org

Meetings and Housing
Heidi Prange | Extension 1424 | heidi@toxicology.org

Meetings (Ancillary)
Jacquelyn Anderson | Extension 1456 | jacquelyn@toxicology.org

Membership
Kimberly von Brook | Extension 1600 | kimberly@toxicology.org

Past Presidents' 5K Fun Run/Walk
Jacquelyn Anderson | Extension 1456 | jacquelyn@toxicology.org

Postdoctoral Scholars
Rachel Woodson | Extension 1602 | rachelw@toxicology.org

Regional Chapters
Ashley Black | Extension 1402 | ashley@toxicology.org

Registration
Jim Dailey | Extension 1428 | jimd@toxicology.org

Scientific Program
David Rossé | Extension 1438 | davidr@toxicology.org

SOT Global Partners
Marcia Lawson | Extension 1446 | marcia@toxicology.org

Special Interest Groups
Ashley Black | Extension 1402 | ashley@toxicology.org

Specialty Sections
Raul Suarez | Extension 1461 | raul@toxicology.org

Support Opportunities
Laura Helm | Extension 1403 | laura@toxicology.org

Undergraduate Students
Rachel Woodson | Extension 1602 | rachelw@toxicology.org

Volunteer Information
Rosibel Alvarenga | Extension 1432 | rosibel@toxicology.org

The SOT 57th Annual Meeting and ToxExpo will be held at the Henry B. González Convention Center located at 900 E. Market Street in downtown San Antonio. *For information on San Antonio restaurants, attractions, and more, go to www.visitsanantonio.com/2018-sot.*

Business Center

Tel: 210.258.8950
Email: store4180@theupsstore.com

The Henry B. González Convention Center UPS Business Center is located in the Market Street Lobby across from the main entrance. The business center offers services such as shipping via DHL or UPS; common office supplies; and high-quality full-color and black-and-white copying, printing, and uploading of documents from a memory stick or CD.

Business Center Hours:

Saturday	9:00 AM–5:00 PM
Sunday	Closed
Monday–Friday	8:00 AM–6:30 PM

Child-Care Services

Child-care services are not provided during the Annual Meeting. Arrangements may be made by contacting the concierge desk at your hotel. Children are not permitted in session rooms, the Exhibit Hall, or the poster area.

Coat/Luggage Check

For your convenience, a coat/luggage check will be available near the Main Lobby. There will be a fee of $3 per item checked. Laptops, cameras, and other electronics will not be accepted.

Hours of Operation:

Sunday	7:00 AM–9:00 PM
Monday	7:00 AM–6:00 PM
Tuesday	7:00 AM–6:00 PM
Wednesday	7:00 AM–6:00 PM
Thursday	7:00 AM–12:00 Noon

Coat/Luggage Check hours are subject to change.

Convention Center Maps and Info

Maps of the convention center, as well as room information for sessions and services, are available in the SOT Mobile Event App.
See the ad on page 2 for details on downloading the app.

First Aid and Emergency Services at the Convention Center

If an emergency should occur while at the Henry B. González Convention Center, courtesy phones are located around the facility to contact the Public Safety Office or call 210.207.7773. You will be connected directly to the 24-hour manned public safety dispatcher at the convention center.

A first-aid room will be located inside entrance to Hall 1.

Hours of Operation:

Saturday	12:00 Noon–7:00 PM
Sunday	6:00 AM–9:00 PM
Monday	7:00 AM–6:00 PM
Tuesday	7:00 AM–6:00 PM
Wednesday	7:00 AM–6:00 PM
Thursday	7:00 AM–12:00 Noon

Please note that in accordance with regulations, the first-aid administrator is not permitted to dispense any medication.

Guest/Spouse Hospitality Room

The SOT Guest/Spouse Hospitality Room will be located in the Grand Hyatt San Antonio. The Hospitality Room provides guest registrants (nonscientists) with a place to meet and socialize with other guests. The room will be open Sunday through Thursday, and information on local attractions will be available. Guests and spouses must be registered for the Annual Meeting to access the Hospitality Room. Guests must register for the Annual Meeting with the person they are accompanying. Registration information is available on page 23.

Internet Access at the Convention Center

Located near Registration, the @SOT Center contains internet-connected computers for attendee use.

@SOT Center—Internet Access

SOT will provide computers you can use to access the internet. These computers are available to attendees in the @SOT Center, located near the Registration Desk.

Free Wireless Internet Access

As a service to Annual Meeting attendees, SOT will be providing free wireless internet access in designated areas of the Henry B. González Convention Center.

Letter of Attendance

Please stop by Registration after Tuesday afternoon if you would like a letter of attendance for your participation in the 2018 SOT Annual Meeting and/or the Continuing Education course(s). If you were unable to pick up your attendance letter, you may send your request to sotmeetings@toxicology.org.

Lost and Found

Lost and found articles should be taken to the SOT Headquarters Office in the convention center. Any items left in the office after 12:00 noon, Thursday, March 15, will be returned to SOT Headquarters. If posters are not removed at the end of the Poster Sessions, on Monday and Tuesday, they will be placed in a poster retrieval area near that Poster Session's presentation area and can be picked up by the author the following morning. Any posters in the retrieval area that are unclaimed by 10:00 am the day following the poster presentation will be destroyed. On Wednesday, posters left on the boards after 5:00 pm will be removed and placed on tables outside the ToxExpo entrance. Any posters unclaimed by 10:00 am on Thursday will be destroyed. If you have any questions regarding these policies, please contact the SOT Headquarters Office.

Media Support Services

SOT welcomes accredited representatives of media organizations to its Annual Meeting. Attending media representatives receive complimentary registration for the meeting, and interviews can be arranged with SOT Council members, meeting speakers and presenters, and SOT general members. For more information, please contact Michelle Werts by email michelle@toxicology.org or call 703.438.3115.

Scientific Poster Printing Services

SOT is pleased to offer poster presenters a convenient printing service through Shepard Exposition Services, the official general service contractor for the SOT Annual Meeting and ToxExpo. Shepard will produce your poster for a reasonable price (rates available on the Poster Printing Order Form on the Annual Meeting website), which will include transportation and storage for the show. Preordered posters should be picked up on-site at the Exhibitor Service Center in the ToxExpo Exhibit Hall.

The deadline to take advantage of this service is February 19, 2018. To place an order for poster printing, complete the Poster Printing Order Form (available on the Annual Meeting website in the Presenters section under On-Site Resources) and email it to houston@shepardes.com. For further information, contact Shepard at 832.799.5700, Monday–Friday 8:00 am–5:00 pm (CT).

View and Upload ePosters

Posters will be available for viewing in the SOT Mobile Event App starting in February 2018. Poster Session presenters will receive instructions for uploading posters in February. Visit the Speaker Ready Room in San Antonio for upload assistance.

SOT Headquarters Office

The SOT Headquarters Office is located in the Henry B. González Convention Center. SOT leadership and staff utilize this office to conduct SOT business while on-site. Attendees are encouraged to visit the office to receive assistance with the SOT Mobile Event App or for general inquiries and assistance.

Hours of Operation:

Saturday	4:00 PM–6:00 PM
Sunday	7:00 AM–5:30 PM
Monday	7:00 AM–5:30 PM
Tuesday	7:00 AM–5:30 PM
Wednesday	7:00 AM–5:30 PM
Thursday	7:00 AM–12:00 Noon

SOT Pavilion

Stop by the SOT Pavilion anytime during ToxExpo hours. Get answers to SOT questions and catch up with friends and colleagues. You can:

- Chat with *Toxicological Sciences* Editor-in-Chief Gary Miller and Managing Editor Virginia Hawkins.
- Share your Annual Meeting, SOT, and toxicology experiences as part of the GSLC #YouTox campaign.
- Learn about SOT activities, programs, and membership.

You always are welcome at the SOT Pavilion. See you there!

The *Program*

The *Program* is the official guide to all the activities of the 2018 Annual Meeting and ToxExpo. The *Program* includes detailed information on the Scientific Sessions, including an overview for these sessions, with the exception of the Poster and Platform Sessions. The *Program* includes the Poster Session schedule and a map of the Poster Sessions, as well as an overview of all the Continuing Education course offerings.

Copies of the *Program* can be picked up on-site. The printed *Program* will be mailed ONLY by request for a fee (within the US and Canada only). If you wish to receive your printed *Program* before the meeting (request made by February 9), please select the "I want to receive the printed *Program* before the meeting by mail" checkbox on the registration form, and the *Program* will be mailed in late February (in the US and Canada only). The *Program* PDF is available for download via the SOT website in February.

All of the information available in the *Program* also is available in the SOT Mobile Event App (see page 2 for details).

Scientific ePosters

SOT is pleased to offer poster presenters the opportunity to share their research electronically as well as in their assigned Poster Sessions. Poster presenters will be able to upload their ePosters beginning in mid-February. ePosters will be available to meeting attendees exclusively through the SOT Mobile Event App until May 15, 2018.

The Toxicologist: The Official Record of the 2018 Annual Meeting Abstracts

The Toxicologist is an important scientific resource, as it is the official compilation of all accepted abstracts for the 57th Annual Meeting of the Society of Toxicology. With 2,500 abstracts for the meeting, this supplementary issue of *Toxicological Sciences* is a critical publication to access the latest findings in toxicology.

- A copy of the printed version of *The Toxicologist* may be purchased for $50 by preordering via the registration form or on-site while supplies last.
- *The Toxicologist* PDF is available for download via the SOT website.
- Full abstracts can be accessed via the SOT Mobile Event App or Online Planner.
- Late-breaking abstracts are available in the *The Toxicologist: Late-Breaking Supplement*, available in early March as a PDF only.

Discover San Antonio, Texas

SOT's trip to San Antonio coincides with the 300th anniversary of the city's official founding, although the Payaya Indians settlements on the site date earlier.

A picturesque city in the heart of Texas, San Antonio hosts a vibrant mix of culture, cuisine, legendary architecture, and history. The Henry B. González Convention Center and SOT hotels are in downtown San Antonio, which also boasts the Alamo, River Walk and San Antonio River, Military Plaza, and the Main Plaza, which dates to the early 1700s. In terms of dining and nightlife, more than 50 restaurants and other establishments in downtown San Antonio will offer discounts to SOT meeting attendees through the "Show Your Badge" program.

For more information about discounts and things to do in San Antonio, go to www.visitsanantonio.com/2018-sot.

Green Initiatives in San Antonio

San Antonio is committed to greening the community through its SA2020 initiative. The mission of SA2020 is to catalyze the entire San Antonio community into passionate, focused, and sustained action to achieve the shared goals that will transform San Antonio into a world-class city by the year 2020 in 11 key vision areas. As part of the "Environmental Sustainability" vision area, the city aims to: build a 21st-century urban energy infrastructure; create a multi-tech venture capital fund; create a green jobs program; adopt a green, high-performance building code for new residential and commercial construction; build a green retrofit program for existing homes and buildings; create an integrated, efficient multi-modal transportation system; engage in municipal facility tree planting; and provide an employee sustainability education program.

Green Initiatives in the Convention Center

In choosing its meeting sites, SOT is dedicated to choosing partners that share its commitment to green meeting practices. The Henry B. González Convention Center engages in green initiatives, such as:

- Waste reduction through the recycling of items such as cardboard, polyurethane foam, wooden pallets, scrap metal, paper, glass, plastics, and aluminum.
- Energy conservation through reducing the settings on or turning off lights, air conditioning, and escalators when areas of the building are not in use. After the implementation of a system efficiencies initiative in 2011, electrical consumption of the building was reduced by 35%.
- Converting food waste into a more environmentally friendly form. The convention center's RK Catering Group has installed 2 Eco-Safe Digesters which use a highly refined formula of microorganisms to decompose carbon-based food waste into a non-toxic liquid that is safely disposed into standard wastewater disposal systems.
- Donating unused prepared food (within established guidelines) to local food banks for distribution to those less fortunate. Food donations are provided to Daily Bread Ministries and the San Antonio Food Bank, with an average of 1,000 meals a month.

Awards and Fellowships

AWARDS CEREMONY
Sunday, March 11, 2018 • 5:15 PM to 6:30 PM
Music Starting at 4:45 PM

Awards Ceremony Music

Sunday, March 11, 4:45 PM to 5:15 PM

Performed by Randy Cordero

Randy Cordero, also known as "El Garrobo," is a flamenco guitarist based in San Antonio. He studied the art of flamenco both in Spain and in the US. His musical style is a blend of traditional Jerez-style flamenco with some contemporary influences.

Awards Ceremony

Sunday, March 11, 5:15 PM to 6:30 PM

Please join the Awards Committee, in conjunction with SOT Council, the Board of Publications, and the Education Committee, as distinguished scientists are honored during the prestigious SOT Awards Ceremony. At the ceremony, SOT Awards are presented, as well as a number of grants, fellowships, and other honors for cutting-edge and novel research. Please refer to the Awards and Fellowships section of the SOT website for complete details at www.toxicology.org/awards.

Endowment Fund 2017 Awards

The Endowment Fund Awards are conferred throughout the Annual Meeting. SOT Endowment Award recipients are recognized through picture displays during the Awards Ceremony Music. SOT Endowment Funds have a mission of assisting in advancing the science of toxicology by providing financial support for the Society's programs. The vision for the SOT Endowment Fund is to establish and increase in net worth a set of Endowment Funds that will provide significant, stable, long-term financial support to aid in achieving the Society's strategic objectives. To learn more, visit www.toxicology.org/endowment.

Upcoming Award Announcements

Regional Chapter, Special Interest Group, and Specialty Section Awards

Regional Chapters, Special Interest Groups, and Specialty Sections offer awards throughout the year. Visit the SOT website for full details at www.toxicology.org/awards. Recognition and presentation of these awards will occur during Regional Chapter, Special Interest Group, and Specialty Section meetings and receptions in San Antonio.

SOT/SOT Endowment Fund/IUTOX Travel Awards

Administered by IUTOX, several travel awards are offered to individuals from countries where toxicology is underrepresented to allow them to attend the SOT Annual Meeting. Award recipients will be honored during the Awards Ceremony.

Outstanding Graduate Student Leadership Committee Award

The Outstanding Graduate Student Leadership Committee Award recognizes student representatives who have contributed to the Society in a significant manner (i.e., above and beyond the normal expected basic service as a representative). Academic achievements are not considered for the award. Representative nominations and support letters should be submitted by February 1. The recipients will be honored during the Student/Postdoctoral Scholar Mixer on Sunday, March 11.

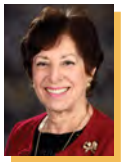
SOT Honors and Awards

Achievement Award

Dana C. Dolinoy, PhD
University of Michigan School of Public Health, Ann Arbor, MI

Founders Award

Ruth A. Roberts,
PhD, ATS, FBTS, ERT, FRSB, FRCPath
ApconiX, Alderley Edge, United Kingdom



Arnold J. Lehman Award

Linda S. Birnbaum, PhD, DABT, ATS
NIEHS, Research Triangle Park, NC

Merit Award

Robert J. Kavlock, PhD
Washington, DC

Merit Award Lecture
Tuesday, March 13, 12:30 PM to 1:30 PM

Distinguished Toxicology Scholar Award

Roger O. McClellan, DVM, DABT, DABVT, ATS
Toxicology & Human Health Risk Analysis, Albuquerque, NM

Distinguished Toxicology Scholar Award Lecture
Monday, March 12, 12:30 PM to 1:30 PM

Public Communications Award

Maureen R. Gwinn, PhD, DABT, ATS
US EPA, Washington, DC

Education Award

Judith T. Zelikoff, PhD
New York University School of Medicine, Tuxedo Park, NY

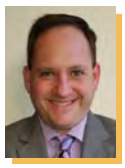
Translational Impact Award

Jia-Sheng Wang, PhD
University of Georgia, Athens, GA

Translational Impact Award Lecture
Tuesday, March 13, 11:00 AM to 12:00 Noon

Enhancement of Animal Welfare Award

Anna B. Lowit, PhD
US EPA, Washington, DC



Undergraduate Educator Award

Joshua P. Gray, PhD
US Coast Guard Academy, New London, CT

Toxicological Sciences Paper of the Year Award

Modeling Compound-Induced Fibrogenesis *In Vitro* Using Three-Dimensional Bioprinted Human Liver Tissues

Toxicological Sciences 154, no. 2 (December 2016): 354–367. https://doi.org/10.1093/toxsci/kfw169.

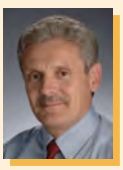
Leah M. Norona, Deborah G. Nguyen, David A. Gerber, Sharon C. Presnell, and Edward L. LeCluyse

Global Senior Scholar Exchange Program

Scholar:
Aina O. Adeogun, PhD
University of Ibadan, Ibadan, Nigeria

Host:
Augustine Arukwe, DSc
Norwegian University of Science and Technology, Trondheim, Norway

Scholar:
Hilmi Orhan, PhD, ERT
Ege University, Izmir, Turkey



Host:
Hartmut Jaeschke, PhD, ATS
University of Kansas Medical Center, Overland Park, KS

Best Postdoctoral Publication Awards

Presented at the Postdoctoral Assembly Luncheon on Tuesday

Colette N. Miller, PhD
US EPA, Research Triangle Park, NC

Miller, CN, JA Dye, AD Ledbetter, MC Schladweiler, JH Richards, SJ Snow, CE Wood, A Henriquez, LC Thompson, A Farraj, M Hazari, and UP Kodavanti. 2017. **"Uterine Artery Flow and Offspring Growth in Long-Evans Rats Following Maternal Exposure to Ozone During Implantation."** *Environmental Health Perspectives* (accepted for publication).

Sreenivasa C. Ramaiahgari, PhD
NIEHS, Research Triangle Park, NC

Ramaiahgari, SC, S Waidyanatha, D Dixon, M DeVito, R Paules, and S Ferguson. 2017. **"Three-Dimensional (3D) HepaRG Spheroid Model with Physiologically-Relevant Xenobiotic Metabolism Competence and Hepatocyte Functionality for Liver Toxicity Screening."** *Toxicological Sciences* 159, no. 1 (September): 124–136. https://doi.org/10.1093/toxsci/kfx122.

Priyanka Trivedi, PhD
Harvard Medical School, Boston, MA

Ramaiahgari, SC, S Waidyanatha, D Dixon, M DeVito, R Paules, and S Ferguson. 2017. **"Targeting Phospholipase D4 Attenuates Kidney Fibrosis."** *Journal of the American Society of Nephrology.* https://doi.org/10.1681/ASN.2016111222.

Perry J. Gehring Diversity Student Travel Award

Presented at the Committee on Diversity Initiatives Reunion on Saturday

Kimberly A. Rivera-Caraballo
University of Puerto Rico at Humacao, Humacao, PR

SOT Undergraduate Intern Travel Award

Natalie Alvarez
Clemson University, Clemson, SC

Institution where research was conducted:
University of Montana

Supported Grants, Fellowships, and Awards

Colgate-Palmolive Grant for Alternative Research

Kristen Comfort, PhD
University of Dayton, Dayton, OH

Valentina Galbiati, PhD
University of Milan, Milan, Italy

Colgate-Palmolive Award for Student Research Training in Alternative Methods

Ian Huck, BS
University of Kansas Medical Center, Kansas City, KS

Lauren Lewis, BS
Texas A&M University, College Station, TX

Colgate-Palmolive Postdoctoral Fellowship Award in *In Vitro* Toxicology

Recipient to Be Announced

Pfizer SOT Undergraduate Student Travel Awards

Alyssa Bellomo
Kean University, Union, NJ
Institution where research was conducted:
Rutgers, The State University of New Jersey

Colin Cess
University at Buffalo, Buffalo, NY
Institution where research was conducted:
Boehringer Ingelheim

Irisyunuel L. Hernandes
North Carolina Central University, Durham, NC

Rabia Javed
John Jay College of Criminal Justice, New York, NY

Yoomin Jo
Baylor University, Waco, TX

Emily Measel
University of Georgia, Athens, GA

Ricardo Navarro
University of Puerto Rico at Mayaguez, Mayaguez, PR
Institution where research was conducted:
Rutgers, The State University of New Jersey

Jacob A. Noeker
College of Idaho, Caldwell, ID

Claire Otero
College of Idaho, Caldwell, ID

Brittany Rickard
University of the Sciences, Philadelphia, PA
Institution where research was conducted:
Rutgers, The State University of New Jersey

Adrianna Suazo
Northern New Mexico College, Española, NM
Institution where research was conducted:
Michigan State University

Jennifer Tao
Rutgers, The State University of New Jersey, Piscataway, NJ

Steven J. Toro De León
University of Puerto Rico at Humacao, Humacao, PR
Institution where research was conducted:
University of Connecticut

Makeba Walcott
Vassar College, Poughkeepsie, NY
Institution where research was conducted:
Oregon State University

Syngenta Fellowship Award in Human Health Applications of New Technologies

Sharavan Ramachandran, PhD
Texas Tech University Health Science Center, Amarillo, TX

SOT | Society of Toxicology

SOT | Society of Toxicology ENDOWMENT
Investing in the Future ...

Awards & Fellowships

Call for 2019 Nominations

More than 200 distinguished toxicologists, postdoctoral researchers, and students are honored each year.

Submit your nominations by October 9, 2018.

www.toxicology.org/awards

You can tell the stories of the science and events of the 2018 meeting.

Become an SOT Reporter.

Contact michelle@toxicology.org to sign up and for more information.

Events and Activities

All activities will be held at the Henry B. González Convention Center, unless otherwise noted.

Welcome Reception

Sunday, March 11, 6:30 PM to 7:30 PM

The Welcome Reception is a great opportunity to renew friendships and to make new acquaintances. Please join the Society in this kick-off of the Annual Meeting.

25-Year (Or More) Member Reception

Sunday, March 11, 7:00 PM to 8:00 PM

If you have been a member of the Society of Toxicology for 25 years or more, please join your colleagues in recognition and celebration of your contributions to the Society. Be sure to wear your membership anniversary pin.

Request Meeting Space

Ancillary meetings, hospitality suites, satellite meetings, and 24-hour room holds can be arranged through the SOT Meetings Department. Meeting requests must be received by January 4, 2018, to be listed in the *Program*.

Visit the SOT Annual Meeting website to view the policies and access the application form.

Global Gallery of Toxicology

Monday, March 12 to Wednesday, March 14, 9:15 AM to 4:30 PM

Toxicology societies from around the world are invited to participate in the Global Gallery of Toxicology. Now in its seventh year, posters of these sister societies will be prominently displayed during the meeting, showcasing their formation, key accomplishments, strategic initiatives, and activities. Meet representatives of these organizations from 11:45 am to 12:15 pm on Monday, March 12. Posters will be available for viewing during the ToxExpo hours. The goal of SOT and of all these societies is to increase the reliance of international decision makers on the science of toxicology and to advance human health and disease prevention. For more information about participating in the Global Gallery, please contact Kevin Meritt by email kevin@toxicology.org by January 6, 2018.

Regional Chapter, Special Interest Group, and Specialty Section Posters

Monday, March 12 to Wednesday, March 14, 9:15 AM to 4:30 PM

Dedicated poster space is available for the SOT Regional Chapters, Special Interest Groups, and Specialty Sections during the 2018 SOT Annual Meeting. The poster area will be located adjacent to the SOT Pavilion in the ToxExpo Exhibit Hall. Come meet representatives on Monday, March 12, from 11:45 am to 12:15 pm. Posters will be available for viewing during the ToxExpo hours.

Global Collaboration Coffee

Monday, March 12, 9:30 AM to 11:30 AM

IUTOX invites all Global Gallery participants and representatives of societies from around the world to the Global Collaboration Coffee hosted by SOT. This event offers an opportunity for scientific leaders to connect and gain a better understanding of the initiatives of societies around the world. Following the coffee, attendees will adjourn together to the Global Gallery, where presenters will share their posters in a "Representative Attended" poster time from 11:45 am to 12:15 pm on Monday, March 12. Please see previous page for additional information about the poster display. Please contact Kevin Merritt by email kevin@toxicology.org for participation information in the Global Collaboration Coffee and Global Gallery.

Past Presidents' 5K Fun Run/Walk

Tuesday, March 13, 7:00 AM
Hemisfair Park

Supported by:
IDEXX BioResearch

When you pack for the meeting, don't forget your running shoes so you can join the eighth annual Past Presidents' 5K Fun Run/Walk! Open to anyone interested, this event is a great opportunity to meet old friends and make new acquaintances in a casual environment, joining SOT's Past Presidents in showing support for SOT. Whether you're in it for some friendly competition or would rather take a leisurely stroll, this event's emphasis is on camaraderie and will bring together runners and walkers of all levels and paces.

Register by February 12 to receive a complimentary souvenir t-shirt; visit the Program section of the SOT Annual Meeting website to register. Registration is only $25, and all proceeds support the SOT Endowment Fund. Visit the Annual Meeting website to register.

SOT Annual Business Meeting

Tuesday, March 13, 4:45 PM to 6:15 PM

SOT Members are invited and encouraged to attend the SOT 57th Annual Business Meeting. The agenda includes discussion of plans for next year, a financial summary, and a review of the 2017–2018 accomplishments.

Tox ShowDown

Tuesday, March 13, 7:30 PM to 9:00 PM
Location to Be Announced

Chairperson(s): *Phil Wexler, NIH-NLM, Bethesda, MD.*

This is the seventh year of the Tox ShowDown, the toxicological quiz game par excellence. Three teams of three contestants each—the Endocrine Disruptors, the Free Radicals, and the Toxic Metabolites—battle each other to answer questions wholly, partially, or remotely related to toxicology. Topics cover the gamut, including the role of toxicology in history, current events, arts, culture, and society, not to mention science. The event features a cash bar and is a great opportunity to see how many questions you can answer correctly, while enjoying a good laugh. As always, there will be prizes for all participants and audience door prizes.

Undergraduate Educator Network Meeting

Date and Time to Be Announced

Chairperson(s): *Larissa Williams, Bates College, Lewiston, ME.*

Endorser(s):
Education Committee
Undergraduate Education Subcommittee

The Education Committee and the Undergraduate Education Subcommittee are hosting the Undergraduate Educator Network Meeting for all faculty involved in the teaching of toxicology to undergraduates, trainees thinking about teaching, and those interested in including toxicology at the undergraduate level. Hear an update on initiatives for undergraduate faculty, provide your input on these activities and the draft toxicology learning objectives, and discuss shared interests in breakout groups.

Undergraduate Diversity Program

Saturday, March 10 to Monday, March 12
Marriott Rivercenter

Chairperson(s): *Kimberly Hodge-Bell, Monsanto Company, St. Louis, MO.*

Hosted by:
Committee for Diversity Initiatives (CDI)

Recipients of the Undergraduate Diversity Program Student and Advisor Travel Awards participate in a three-day program to learn more about toxicology and careers in biomedical research. The program begins Saturday evening with networking within mentor groups, an introduction to toxicology, and the CDI Reunion, a celebration including current and past program participants and organizers. See the description at right for the Sunday program. On Monday, the students participate in Scientific Sessions; visit Poster Sessions; attend the *In Vitro* Lecture and Luncheon; continue to network with graduate students, postdoctoral scholars, and career toxicologists; and conclude this concentrated exposure to the discipline of toxicology and possibilities inherent in the pursuit of graduate studies in the biomedical sciences. For schedule details, go to www.toxicology.org/am-undergraduates.

Sunday Undergraduate Education Program

Sunday, March 11, 8:00 AM to 5:00 PM
Marriott Rivercenter

Chairperson(s): *Kimberly Hodge-Bell, Monsanto Company, St. Louis, MO.*

Hosted by:
Committee for Diversity Initiatives (CDI)

Endorser(s):
Education Committee
Undergraduate Education Subcommittee

Any undergraduate student who attends the Annual Meeting is invited to register for the Sunday Undergraduate Education Program. The schedule for the day includes introductory presentations in different areas of toxicology, including an opportunity to explore and interpret data.

Students discuss with graduate students and academic program directors how to submit strong graduate school applications and succeed in graduate school, as well as learning the merits of specific graduate programs. They also network with SOT mentors and toxicologists in various employment sectors to become more familiar with different career paths in toxicology. For schedule details, go to www.toxicology.org/am-undergraduates.

Student/Postdoctoral Scholar Mixer

Sunday, March 11, 7:30 PM to 9:00 PM

(Ticket Required)

Hosted by:
Graduate Student Leadership Committee (GSLC)

This is an opportunity for all students and postdoctoral scholars to gather, meet new colleagues, and reestablish relationships in an informal atmosphere at the beginning of the meeting. Learn about being involved in SOT by speaking with student leaders at the SOT component group posters. The GSLC Outstanding Leadership Award is presented during this event. Tickets are obtained at no cost by registering for the Mixer on the Annual Meeting Registration Form. Ticket and meeting badge are required. Complimentary refreshments and a cash bar will be available.

Committee on Diversity Initiatives Reunion

Saturday, March 10, 7:30 PM to 8:30 PM
Marriott Rivercenter

Hosted by:
Committee for Diversity Initiatives (CDI)

Join the Committee on Diversity Initiatives as it celebrates the Undergraduate Diversity Program and the people who make it successful. The CDI Reunion is a great opportunity for former students, organizers of the program, and volunteers to gather and celebrate 29 years of success in encouraging the next generation of scientists. Please welcome and network with this year's undergraduate student participants. The program will include the presentation of the 2018 Perry J. Gehring Diversity Student Travel Award. Dessert, coffee, and tea will be served, so please mark your calendars and start the 57th Annual Meeting with a fun and interactive evening at the CDI Reunion.

In Vitro Toxicology Lecture and Luncheon

More Than Skin Deep: When Alternative Approaches Outperform Animal Tests

Monday, March 12, 11:30 AM to 1:00 PM

(Ticket Required)

Chairperson(s): *Mindy Reynolds, Washington College, Chestertown, MD.*

Lecturer: *Nicole Kleinstreuer, NIEHS, Research Triangle Park, NC.*

Supported by:
An Educational Grant from
The Colgate-Palmolive Company

Hosted by:
Education Committee

The goal of the *In Vitro* Toxicology Lecture series is to feature important research using *in vitro* and alternative techniques to study basic mechanisms and to develop test methods aimed at replacing animal use whenever feasible. Undergraduate students, graduate students, postdoctoral scholars, and recipients of Colgate-Palmolive awards are among the guests at the *In Vitro* Toxicology Lecture and Luncheon. Students and postdoctoral scholars register for $10 (nonrefundable) via the Annual Meeting registration process.

Dr. Kleinstreuer will present challenges in developing and receiving regulatory acceptance of non-animal testing approaches for skin sensitization. Skin sensitization, or allergic contact dermatitis, is a toxicity endpoint of widespread relevance. With legislation prohibiting the use of animal-based testing for cosmetic ingredients and concern about poor reproducibility and predictive performance of these tests, alternative methods for predicting key events in the adverse outcome pathway have been developed which have equivalent or superior performance to the traditional murine local lymph node assay. The challenges and benefits will be explored in discussions at each table.

Postdoctoral Assembly Luncheon

Tuesday, March 13, 12:20 PM to 1:20 PM

(Ticket Required)

Chairperson(s): *Samantha J. Snow, US EPA, Chapel Hill, NC.*

Hosted by:
Postdoctoral Assembly (PDA)

The Postdoctoral Assembly Luncheon is a casual event that encourages engagement and networking among postdoctoral scholars. Finishing up a discussion from your morning poster session? Leaving early to set up a poster or attend another meeting? That's no problem; stop in when you can! Enjoy a buffet lunch while networking with others, including PDA officers, Postdoctoral Representatives, and SOT Councilor members. This is the time for postdocs to relax, celebrate achievements, and have fun. At 12:45 pm, there will be a short program which will include recognition of the Best Postdoctoral Publication Award recipients and the welcoming of the 2018–2019 PDA officers. Door prizes add even more fun to this lively event. Postdocs should reserve a ticket for $10 when registering for the Annual Meeting.

Career Exploration through Speed Informational Interviews

Tuesday, March 13, 1:25 PM to 2:45 PM

(Ticket Required)

Hosted by:
Postdoctoral Assembly

Do you find yourself wondering what your career options are in the field of toxicology? Then this is the event for you! This career development special event is designed for graduate students and postdocs who want to gain insight into the different career sectors in toxicology. Groups of trainees will rotate through a series of approximately eight-minute discussions with career representatives from academia, government, and industry. Trainees can ask the career representatives questions about their background, career path, the hiring process in their company/sector, and other aspects of identifying and pursuing career interests. This session will provide an informal opportunity to gain insight about different employment sectors in toxicology through candid discussions in a casual setting. Graduate students and postdocs are encouraged to register early, as registration will be limited to maximize the opportunity for small-group discussion with career representatives.

Undergraduate Student Meeting

Date and Time to Be Announced

Chairperson(s): *Wade Powell, Kenyon College, Gambier, OH; and Larissa Williams, Bates College, Lewiston, ME.*

Hosted by:
Education Committee
Undergraduate Education Subcommittee

Undergraduate students are encouraged to participate in an informal meeting to talk about shared interests related to career paths in toxicology, discuss undergraduate tox-related activities, and provide feedback to the Undergraduate Education Subcommittee. Most of the meeting will be devoted to small-group interaction with graduate students and postdoctoral scholars who can provide perspective and answer questions about toxicology graduate programs, getting started in a toxicology job, and career options available to those with toxicology degrees.

Book your hotel reservation today!

Reserve early to secure the best rates. Go to www.toxicology.org/housing or call SOT's official housing company: Connections Housing, 800.262.9974 or 404.842.0000.

The deadline is February 21, 2018.
See details on page 17.

Education-Career Development Opportunities

Chat with an Expert

Monday, March 12 to Thursday, March 15
Time Varies by Group

(Meet at the Chat with an Expert Poster Board in the Main Lobby)

Hosted by:
Graduate Student Leadership Committee

The purpose of Chat with an Expert is to provide graduate students and postdoctoral scholars with the opportunity to network informally with well-established toxicologists while obtaining career advice and meeting new colleagues. Small groups are composed by matching research interests of students and postdocs with those of an expert. The expert for each group identifies a time and a place for an informal meeting, and the group meets at the Chat with an Expert Poster before proceeding to the meeting location. This program also includes opportunities for postdocs to host informal meetings with graduate students. Expert registration generally opens in December; graduate student/postdoc registration will open in early 2018. Details for each group meeting will be sent to participants in advance of the meeting.

Poster Tours for Trainees

Monday, March 12 to Wednesday, March 14
Time Varies by Group

(Meet at the Poster Tour Board in the Main Lobby)

Hosted by:
Postdoctoral Assembly

The Postdoctoral Assembly organizes Poster Tours for Trainees for graduate students and postdoctoral scientists to participate in a one-hour guided poster tour with an expert toxicologist. These small group tours provide the opportunity for trainees to take part in critical evaluation of cutting-edge toxicology methods and research findings and network with an expert toxicologist. Recruitment of individuals interested in being poster tour guides begins in early December. Graduate student and postdoctoral scholar sign-up will open in early 2018. Details for each group will be distributed to the participants in advance of the meeting.

Trainee Discussion with Plenary Session Presenter: Dr. Porteus

Monday, March 12, 9:45 AM to 10:45 AM

(Ticket Required; Limited Seating)

Presenter: *Matthew H. Porteus, Stanford University, Stanford, CA.*

Dr. Porteus will meet informally for discussion with graduate students and postdoctoral scholars after the Plenary Session *(see page 69)*. Registration is limited to SOT student and postdoctoral members.

Trainee Discussion with Medical Research Council (MRC) Lecturer: Dr. Hastings

Wednesday, March 14, 2:00 PM to 3:00 PM

(Ticket Required; Limited Seating)

Lecturer: *Michael Hastings, MRC Laboratory of Molecular Biology, Cambridge, United Kingdom.*

Dr. Hastings will meet informally for discussion with graduate students and postdoctoral scholars after his Keynote MRC Lecture *(see page 69)*. Registration is limited to SOT student and postdoctoral members.

Education-Career Development Sessions

In It to Win It: How to Negotiate During the Interview Process
Tuesday, March 13, 11:00 AM to 12:20 PM

View the full description on page 94.

Perfecting Your "Elevator Speech"
Tuesday, March 13, 4:30 PM to 5:50 PM

View the full description on page 101.

Career Opportunities in Regulatory Toxicology
Wednesday, March 14, 11:00 AM to 12:20 PM

View the full description on page 108.

Research-Based Approaches to Improve Teaching Effectiveness in Toxicology Classrooms
Wednesday, March 14, 4:30 PM to 5:50 PM

View the full description on page 114.

SOT invites its sister societies from around the world to participate in the Global Gallery of Toxicology.

See page 41 for information to sign up.

Calling All Contestants!

An evening of tox trivia and fun as three teams compete to see who knows the most when it comes to toxicological fact and fancy. To participate, contact sothq@toxicology.org.

TOX SHOWDOWN

Tuesday, March 13 | 7:30 PM

Regional Chapter Events

Monday, March 12, through Wednesday, March 14, Various Times and Locations

(Refer to the Annual Meeting Program*, Mobile Event App, or Online Planner for up-to-date details.)*

Many of the SOT Regional Chapters meet during the SOT Annual Meeting. All current and prospective SOT Regional Chapter members are encouraged to attend.

Event	Date	Time
Allegheny-Erie, Michigan, and Lake Ontario Regional Chapters Joint Reception	Monday, March 12	4:45 PM to 6:15 PM
Mid-Atlantic Regional Chapter Business Meeting and Networking Luncheon	Monday, March 12	12:00 Noon to 2:00 PM
National Capital Area and North Carolina Regional Chapters Joint Reception	Monday, March 12	7:00 PM to 9:00 PM
Northeast Regional Chapter Networking Reception	Monday, March 12	5:30 PM to 7:30 PM
Northeast Regional Chapter Student Luncheon	Tuesday, March 13	12:00 Noon to 1:45 PM
Northern California Regional Chapter Reception	Tuesday, March 13	7:00 PM to 10:00 PM
Pacific Northwest Regional Chapter Reception	Monday, March 12	5:30 PM to 7:30 PM

Special Interest Group Events

Monday, March 12, through Wednesday, March 14, Various Times and Locations

(Refer to the Annual Meeting Program*, Mobile Event App, or Online Planner for up-to-date details.)*

Each of the Special Interest Groups will hold a meeting/reception during the 2018 SOT Annual Meeting at various local locations. All current and prospective SOT Special Interest Group members are encouraged to attend.

Event	Date	Time
American Association of Chinese in Toxicology Special Interest Group Distinguished Chinese Toxicologist Lectureship Award and Reception	Monday, March 12	5:00 PM to 9:00 PM
American Association of Chinese in Toxicology Special Interest Group Career Development Workshop	Tuesday, March 13	12:00 Noon to 1:45 PM
Association of Scientists of Indian Origin Special Interest Group Career Talk with Toxperts	Monday, March 12	4:45 PM to 5:45 PM
Association of Scientists of Indian Origin Special Interest Group Reception	Monday, March 12	7:00 PM to 9:00 PM
Hispanic Organization of Toxicologists Special Interest Group Mentoring Activity	Tuesday, March 13	12:00 Noon to 1:00 PM
Hispanic Organization of Toxicologists Special Interest Group Reception	Tuesday, March 13	6:00 PM to 9:00 PM
Korean Toxicologists Association in America Special Interest Group Reception	Monday, March 12	6:00 PM to 9:00 PM
Toxicologists of African Origin Special Interest Group Reception	Monday, March 12	6:00 PM to 7:30 PM
Women in Toxicology Special Interest Group Reception	Wednesday, March 14	4:45 PM to 7:00 PM

Specialty Section Events

Monday, March 12, through Wednesday, March 14, Various Times and Locations

(Refer to the Annual Meeting Program*, Mobile Event App, or Online Planner for up-to-date details.)*

Each of the SOT Specialty Sections will hold either a luncheon or early evening meeting/reception during the 2018 SOT Annual Meeting. All current and prospective SOT Specialty Section members are encouraged to attend.

Event	Date	Time
Biological Modeling Specialty Section Meeting/Reception	Wednesday, March 14	6:00 PM to 7:30 PM
Biotechnology Specialty Section Meeting/Reception	Wednesday, March 14	6:00 PM to 7:30 PM
Carcinogenesis Specialty Section Meeting/Reception	Monday, March 12	6:00 PM to 7:30 PM
Cardiovascular Toxicology Specialty Section Meeting/Luncheon	Monday, March 12	12:00 Noon to 1:30 PM
Clinical and Translational Toxicology Specialty Section Meeting/Reception	Monday, March 12	6:00 PM to 7:30 PM
Comparative and Veterinary Specialty Section Meeting/Luncheon	Tuesday, March 13	12:00 Noon to 1:30 PM
Computational Toxicology Specialty Section Meeting/Luncheon	Tuesday, March 13	12:00 Noon to 1:30 PM
Dermal Toxicology Specialty Section Meeting/Reception	Wednesday, March 14	6:00 PM to 7:30 PM
Drug Discovery Toxicology Specialty Section Meeting/Reception	Tuesday, March 13	6:00 PM to 7:30 PM
Ethical, Legal, Forensics, and Societal Issues Specialty Section Meeting/Luncheon	Wednesday, March 14	12:00 Noon to 1:30 PM
Exposure Specialty Section Meeting/Luncheon	Wednesday, March 14	12:00 Noon to 1:30 PM
Food Safety Specialty Section Meeting/Reception	Tuesday, March 13	6:00 PM to 7:30 PM
Immunotoxicology Specialty Section Meeting/Reception	Tuesday, March 13	6:00 PM to 7:30 PM

Specialty Sections

Event	Date	Time
***In Vitro* and Alternative Methods Specialty Section Meeting/Reception**	**Wednesday, March 14**	**6:00 PM to 7:30 PM**
Inhalation and Respiratory Specialty Section Meeting/Reception	Monday, March 12	6:00 PM to 7:30 PM
Mechanisms Specialty Section Meeting/Reception	**Wednesday, March 14**	**6:00 PM to 7:30 PM**
Medical Device and Combination Product Specialty Section Meeting/Reception	Tuesday, March 13	6:00 PM to 7:30 PM
Metals Specialty Section Meeting/Reception	**Tuesday, March 13**	**6:00 PM to 7:30 PM**
Mixtures Specialty Section Meeting/Reception	Monday, March 12	6:00 PM to 7:30 PM
Molecular and Systems Biology Specialty Section Meeting/Reception	**Monday, March 12**	**6:00 PM to 7:30 PM**
Nanotoxicology Specialty Section Meeting/Reception	Tuesday, March 13	6:00 PM to 7:30 PM
Neurotoxicology Specialty Section Meeting/Reception	**Tuesday, March 13**	**6:00 PM to 7:30 PM**
Occupational and Public Health Specialty Section Meeting/Luncheon	Monday, March 12	12:00 Noon to 1:30 PM
Ocular Toxicology Specialty Section Meeting/Reception	**Monday, March 12**	**6:00 PM to 7:30 PM**
Regulatory and Safety Evaluation Specialty Section Meeting/Reception	Monday, March 12	6:00 PM to 7:30 PM
Reproductive and Developmental Toxicology Specialty Section Meeting/Reception	**Wednesday, March 14**	**6:00 PM to 7:30 PM**
Risk Assessment Specialty Section Meeting/Reception	Tuesday, March 13	6:00 PM to 7:30 PM
Stem Cells Specialty Section Meeting/Reception	**Wednesday, March 14**	**6:00 PM to 7:30 PM**
Toxicologic and Exploratory Pathology Specialty Section Meeting/Luncheon	Tuesday, March 13	12:00 Noon to 1:30 PM

Career Advancement and Development Resources

SOT Mentoring Breakfast

Monday, March 12, 6:15 AM to 7:45 AM

(Ticket Required)

Endorser(s):
Career Resource and Development Committee
Postdoctoral Assembly
Graduate Student Leadership Committee

The Society of Toxicology recognizes the importance of mentoring in the scientific and professional development of its members. As such, the Society is pleased to announce the seventh annual Mentoring Breakfast.

The Mentoring Breakfast is for SOT members at any career stage—from students and scholars to senior scientists—who are seeking a mentor. Trained facilitators will lead small-group discussions to determine each individual's wants and needs in a mentor and then will use this information to connect the participant with an appropriate mentor. Please note that mentor information will be provided after the Annual Meeting, and mentors do not attend the breakfast.

Registration is limited and is accepted on a first-come, first-served basis. Attendance is $10 per person and includes a continental breakfast.

Research Funding Insights

Monday, March 12 to Wednesday, March 14, 9:30 AM to 4:30 PM

Hosted by:
Career Resource and Development Committee

Representatives from federal agencies will be available in the Research Funding Insights Room for individual conversations. Make an appointment with your program officer in advance or check the posted schedule to meet with a staff member who can discuss aspects of scientific review or specific grant opportunities. New investigators are especially encouraged to meet with program staff.

Job Bank

Job Bank access will be available, as always, through your computer or mobile device and at the Annual Meeting @SOT Center. Visit the Job Bank at www.toxicology.org/jobbank. For additional information, contact Kim von Brook by email careerresoures@toxicology.org or call 703.438.3115.

Mentor Match

The objective of the Mentor Match online database is to connect mentees with potential mentors from the SOT membership to provide advice on career-path selection, professional development, and work/life balance topics. SOT members are encouraged to share their professional knowledge and experience by serving as mentors for colleagues and for the next generation of toxicologists.

The SOT Annual Meeting provides a great opportunity for the mentor and mentee to meet in person. SOT members are encouraged to visit the Mentor Match site and register online as mentors and/or mentees. The Mentor Match program is free to all active SOT members. Visit www.toxicology.org/mentormatch.

Education-Career Development Sessions

In It to Win It: How to Negotiate During the Interview Process

Tuesday, March 13, 11:00 AM to 12:20 PM

View the full description on page 94.

Perfecting Your "Elevator Speech"

Tuesday, March 13, 4:30 PM to 5:50 PM

View the full description on page 101.

Career Opportunities in Regulatory Toxicology

Wednesday, March 14, 11:00 AM to 12:20 PM

View the full description on page 108.

Research-Based Approaches to Improve Teaching Effectiveness in Toxicology Classrooms

Wednesday, March 14, 4:30 PM to 5:50 PM

View the full description on page 114.

job bank

Online Job Search and Recruiting Service

Job Seekers

- Find Your Next Career Opportunity
- SOT Members Post Resumes and Search Positions for Free

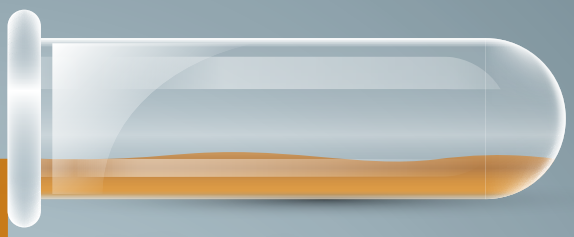
Employers

- Focus Your Hiring Efforts
- Recruit Highly Qualified Candidates

Academia ◇ Government ◇ Industry

www.toxicology.org/jobbank

Organize a Contemporary Concepts in Toxicology (CCT) Meeting



Follow these easy steps to bring cutting-edge science to your colleagues.

01 Your Idea/The Proposal

Explain how your topic is at the forefront of advancing toxicology and related fields.

02 Approval & Seed Money

After working with SOT to fine-tune your proposal and it is accepted, SOT contributes $25,000 to help offset the meeting expenses.

03 Developing the Meeting

You manage the scientific program. SOT handles all logistics: venue, housing, registration, speaker communication, and creating promotional materials.

04 The Meeting

With SOT's assistance, host fantastic scientific presentations and discussions through a face-to-face meeting or a webinar.

05 Shared Benefit

Hosting/organizing Regional Chapters, Special Interest Groups, and Specialty Sections share in the meeting's profits.

SOT | Society of Toxicology

Visit www.toxicology.org/cct to get started.

Satellite Meetings

Each year, SOT endorses several Satellite Meetings that are held in conjunction with the Annual Meeting. Satellite Meetings are organized around scientific topics related to toxicology and will be held in and around the San Antonio area. Visit www.toxicology.org/am-satellite for up-to-date information.

Building a Better Epithelium: Breaking the Barrier to the Next Generation of Toxicity Testing

SOT Contemporary Concepts in Toxicology [CCT] meeting

Saturday, March 10, 8:30 AM to 6:30 PM
Henry B. González Convention Center

(Separate Registration Required)

Hosted by: *Society of Toxicology,* In Vitro *and Alternative Methods Specialty Section, Molecular and Systems Biology Specialty Section, and Regulatory and Safety Evaluation Specialty Section.*

This meeting will provide opportunities for toxicologists that are interested in, or currently using, organotypic models and technology developers to meet face-to-face to foster collaborations that will move the field forward. In addition to presenting the state of the science, this conference will include moderated discussion sessions for attendees and speakers to discuss advances, future needs, and data gaps, and applications of these models in the investigation into the cellular and molecular mechanisms of toxicity.

Visit www.toxicology.org/epithelium to register for this CCT meeting, view the agenda, and find abstract submission information.

Toxicological Concerns in Older Adults, a Neglected Majority

SOT Contemporary Concepts in Toxicology [CCT] meeting

Saturday, March 10, 8:30 AM to 5:30 PM
Henry B. González Convention Center

(Separate Registration Required)

Hosted by: *Society of Toxicology and Scientific Liaison Coalition.*

The primary goal of this meeting is to increase understanding of the changes associated with the aging process and discuss ways in which these changes may influence toxicity outcomes. The discussions will have potential impact on the development of toxicological assessments, the drug development process, and clinical practice.

Visit www.toxicology.org/agingcct to register for this CCT meeting, view the agenda, and find abstract submission information.

Proposing a Satellite Meeting

Proposals should be sent by email to heidi@toxicology.org to the attention of Leigh Ann Burns Naas, SOT vice president and Scientific Program Committee chair. Requests approved by January 4, 2018, will be published in the *Program*. All requests must be received by January 19, 2018.

Participate in Free Toxicology-Related Training by SOT and the US FDA Center for Food Safety and Applied Nutrition

Covering emerging science in food and ingredient safety and held at the US FDA campus, the SOT FDA Colloquia are simulcast and recorded for additional learning opportunities.

Visit www.toxicology.org/fda to sign up for upcoming events and view past colloquia.

Continuing Education

Sunday, March 11, 2018

SR—Sunrise (7:00 AM–7:45 AM)
AM—Morning (8:15 AM–12:00 Noon)
PM—Afternoon (1:15 PM–5:00 PM)

Continuing Education Courses

The Continuing Education (CE) Program offers a wide range of courses that cover established knowledge in toxicology, as well as advanced techniques or approaches for those with experience in the field. Courses can be applied toward certifying and licensing board requirements and also may be used for recertification with the American Board of Toxicology (ABT). General courses are intended to provide a broad overview of an area or to assist individuals in learning new techniques or approaches, while courses based on more specialized topics are intended to be of interest to individuals with previous knowledge of the subject or already working in the field.

All courses will be held at the Henry B. González Convention Center. Please check the signage in the registration area and at the CE booth for room assignments. Note: Links to the electronic CE course books are distributed in advance of the meeting; USB drives containing electronic copies of the CE course books will be available in the room immediately prior to the course (they will not be available at the registration area).

Registration for the Annual Meeting and a separate CE course ticket are required.

CE Books Available Exclusively in Electronic Format

Course registrants will receive information on accessing the electronic CE course book prior to the meeting and/or may pick up a USB drive containing a copy of the electronic book on-site.

Sunday

CRISPR-Cas9 for Toxicologists

Sunday, March 11, 7:00 AM to 7:45 AM
SR01 | SUNRISE MINI-COURSE

Chairperson(s): *Gary W. Miller, Emory University, Atlanta, GA; and Lesa L. Aylward, Summit Toxicology, Falls Church, VA.*

Primary Endorser:
Specialty Section Collaboration and Communication Group

Recent advances in genome editing using CRISPR-Cas9 and related technologies have revolutionized the ability to manipulate genes in a rapid, precise, and flexible manner. These advances have spurred an explosion of interest in the possible ways in which genome editing can improve human health. This course will provide an overview of CRISPR-Cas systems, the structure and function of CRISPR-Cas9, the re-purposing of CRISPR-Cas9 for genome engineering, and recent advances in genome editing and the application of these techniques to toxicology. These include its use in screening the genome in different biological systems for gene pathways related to sensitivity or resistance to chemical toxicity, for elucidating the pathways of biological response to chemical stressors, and other applications related to the understanding of mechanisms of gene-environment interactions. The Emerging Science for Environmental Health Decisions (ESEHD) Standing Committee of the National Academies of Science, Engineering, and Medicine serves as an important link between the National Academies and the Society of Toxicology. To foster this collaboration, the ESEHD Committee is pleased to sponsor this course on the use of advanced genome-editing techniques in toxicology, which follows a planned meeting on gene editing in toxicology and environmental health to be held at the National Academies' Headquarters in January 2018.

The Structure and Function of CRISPR-Cas9. David Taylor, University of Texas, Austin, TX.

Genome-Wide CRISPR Applications in Toxicology. Christopher Vulpe, University of Florida, Gainesville, FL.

The What, When, and How of Using Data from Alternative Testing Methods in Chemical Safety Assessments

Sunday, March 11, 7:00 AM to 7:45 AM
SR02 | SUNRISE MINI-COURSE

Chairperson(s): *Suzanne C. Fitzpatrick, US FDA, College Park, MD; and Mansi Krishan, ILSI North America, Washington, DC.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

Other Endorser(s):
Biological Modeling Specialty Section
Food Safety Specialty Section

In the last decade, the fields of toxicology and risk assessment have undergone an extensive shift towards the development of alternative testing methodologies that potentially can be used to assess the safety of chemicals and reduce animal use in toxicological research. New approaches, including molecular biology, computational and systems biology, high-throughput screening (HTS) assays, automated analytical methods, and robotic implementation, are generating toxicological data at unprecedented speeds. Compared to traditional animal toxicity studies, advanced HTS methods, reach-across approaches, *in silico* tools, and other alternative methodologies hold considerable promise to define biological activity profiles of chemicals. The first step towards better understanding the application of these new methodologies and tools for safety assessment of chemicals is an interdisciplinary approach which: 1) promotes interaction among scientists from diverse backgrounds (e.g., toxicologists, chemists, biologists, mathematicians, programmers, and risk assessors) and 2) provides hands-on-training to demonstrate the utility and challenges associated with the use of these alternative testing methods in different sectors. This course will provide a unique training platform to equip attendees with all the necessary knowledge and know-how to use and apply data from HTS assays, *in silico* tools, and other emerging technologies, such as virtual embryo, in the safety evaluation of chemicals. It is a learning tool aimed at providing training to scientists interested in applying the latest approaches to the safety assessment of chemicals, as well as students and researchers interested in improving the existing methods and developing new alternative methods for toxicological research. The course will include an overview of each of the methodologies (HTS methods, *in silico* tools, virtual embryo) and case study exercises to demonstrate the use of data from these methods and the use of tools in different sectors, such as pharmaceuticals, consumer products, food, agricultural products, and environmental toxicants.

Case Studies on the Use of *In Vitro* Data for Quantitative Evaluation of Dose-Response and Margin of Exposure. Rebecca Clewell, ScitoVation, Research Triangle Park, NC.

Mechanistic Modeling of Developmental Defects through Computational Embryology. Thomas Knudsen, US EPA, Research Triangle Park, NC.

An Introduction to the Basics of Immunotoxicity Testing

Sunday, March 11, 8:15 AM to 12:00 Noon
AM03 | MORNING COURSE

Chairperson(s): *Jamie DeWitt, East Carolina University, Greenville, NC; and Sarah Blossom, University of Arkansas for Medical Sciences, Little Rock, AR.*

Primary Endorser:
Immunotoxicology Specialty Section

The immune system has long been a sensitive target of environmental pollutants, industrial chemicals, and pharmacological agents. For example, several federal laws and guidelines have data requirements for immunotoxicity. However, recent studies by an industry trade association and the the US Environmental Protection Agency Office of Pesticide Programs determined that no clear signs of immunotoxicity may arise from conventional toxicity studies and that additional immunotoxicity testing may only be recommended if "primary indicators" of immunotoxicity arise from conventional toxicity studies. This approach harmonizes with the "weight of evidence" concept that is discussed in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines S8 for human pharmaceuticals and Part 158 for pesticidal substances and certain industrial compounds. This course will provide an overview of the types of immunotoxicity tests often used to meet US data requirements for agents regulated by the US Environmental Protection Agency and the US Food and Drug Administration. The first speaker will set the stage by defining immunotoxicity, discussing the historic aspects of immunotoxicity testing, and highlighting some of the current advances in immunotoxicity assessment, including high-throughput analysis, immunotoxicogenomics, developmental immunotoxicology, and the creation of adverse outcome pathways for immunotoxicity. The second speaker will address the particular data requirements under various laws and guidelines and their applicability to regulatory immunotoxicity. Speaker number three will go into detail about specific required tests under existing laws and guidelines, as well as novel and innovative ways of meeting data requirements. The fourth speaker will provide an overview of the utility of experimental animal models and their predictive value for understanding potential risks toward human health. Finally, the fifth speaker will delve into the information that can be gleaned from human blood samples and how these data can be used to better predict health and disease in exposed/treated humans. Each presentation will include case studies and/or examples of immunotoxicity assessment strategies applied to agents or classes of agents under study, being considered for approval, or under regulatory scrutiny.

An Introduction to Immunotoxicity Testing: Looking to the Past to Inform the Future. Jamie DeWitt, East Carolina University, Greenville, NC.

An Introduction to Immunotoxicity in Risk Assessment. L. Peyton Myers, US FDA, Silver Spring, MD.

Approaches and Methods Used to Generate Useful Immunotoxicity Data. Victor Johnson, Burleson Research Technologies, Inc., Morrisville, NC.

Interpretation of Data from Experimental Animal Studies and Predictive Value for Human Health Risk Assessment. Sarah Blossom, University of Arkansas for Medical Sciences, Little Rock, AR.

Human Immunotoxicology: What Blood and Cells Can Tell Us. Emanuela Corsini, Università degli Studi di Milano, Milan, Italy.

Assessment of Peri- and Prepubertal Developmental and Reproductive Toxicity

Sunday, March 11, 8:15 AM to 12:00 Noon
AM04 | MORNING COURSE

Chairperson(s): *Bethany Hannas, Dow Chemical Company, Midland, MI; and Kary Thompson, Bristol-Myers Squibb, New Brunswick, NJ.*

Primary Endorser:
Reproductive and Developmental Toxicology Specialty Section

Perinatal development through the time of puberty can be particularly vulnerable periods to compound exposures resulting in toxicity. Toxicological assessments during these periods include regulatory-required guideline studies, mode-of-action studies, behavioral and functional assessments, and predictive assays/models. Test guideline-driven study designs covering these periods have evolved over time and are subject to additions or variations, depending on what is known about the tested compound. In addition, the field of toxicology is pushing toward increasingly innovative methods and alternative models, coupled with reduction in animal usage in the assessment of a compound, including during vulnerable developmental periods. As such, multiple study designs and models are utilized to support perinatal and juvenile developmental toxicity assessments of pharmaceutical agents, industrial chemicals, pesticides, food additives, and other environmental contaminants. This course will begin with presentations focused on test guideline-driven study designs and case studies of pharmaceutical and environmental chemical safety assessments during early life stages. The next presentation will cover assessment of functional competence and behavior following compound exposures during these vulnerable development periods. Next, the interpretation, reliability, and reproducibility of these studies will be discussed. The course will conclude with a discussion on looking forward for developmental and reproductive toxicity assessments. This course will discuss alternative models for evaluating reproductive and developmental toxicity and focus specifically on using a zebrafish model as a biosensor for early life stage sensitivity. The course will provide an understanding of current approaches to evaluating compound safety during the critical peri- and postnatal periods of development.

Nonclinical Support of Pediatric Drug Development: A Pharmaceutical Industry Perspective. Sarah Campion, Pfizer, Inc., Groton, CT.

Environmental Chemical Assessments: Multi-Generation and Extended One-Generation Studies. Bethany Hannas, Dow Chemical Company, Midland, MI.

Juvenile Toxicology Neurobehavioral Assessments: When and What Should Be Assessed. Charles Vorhees, Cincinnati Children's Research Foundation and University of Cincinnati, Cincinnati, OH.

Data Interpretation, Reliability, and Reproducibility for DART Studies. Pragati Sawhney Coder, Charles River Laboratories Ashland, LLC, Ashland, OH.

Alternative Models to Detect Developmental and Reproductive Toxicants: Zebrafish as a Case Study. Robert L. Tanguay, Oregon State University, Corvallis, OR.

Biotherapeutic Development: What's behind the Curtain?

Sunday, March 11, 8:15 AM to 12:00 Noon
AM05 | MORNING COURSE

Chairperson(s): *Laura Andrews, AbbVie, Worcester, MA; and Mary Ellen Cosenza, MEC Regulatory & Toxicology Consulting, LLC, Moorpark, CA.*

Primary Endorser:
Biotechnology Specialty Section

Other Endorser(s):
Regulatory and Safety Evaluation Specialty Section

The approval in 1982 of human recombinant insulin began an expansive growth in biotherapeutics. Great successes were achieved and multiple life-altering therapies were developed. Significant guidance has been released by regulatory agencies in the last two decades to help the rational and scientifically-based development of these complex products. The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) S6 guidance, adopted in 1997, was the first document to specifically outline best practices for nonclinical approaches to biologic drug development. Additional guidance documents have since been adopted with regular addendums to reflect scientific advances. Despite 36 years of successful biologic drug development, there remain challenges which need to be addressed on a case-by-case basis for each particular therapeutic agent. As the past has taught us, not all safety issues observed nonclinically are relevant to humans. Likewise, not all human safety issues can be identified nonclinically, especially with poorly designed nonclinical studies or irrelevant animal test systems. In addition to addressing the unique aspects of strategies for developing biologics, this will discuss topics such as the selection of relevant species, the role and interpretation of immunogenicity, and the current regulatory challenges. Selection and evaluation of the most relevant species for biologics programs is fundamental. The role of immunogenicity in nonclinical studies continues to confound and cause concern as to interpretability and translatability of these findings to the clinic. A broad overview will be given of how immunogenicity and other immune responses in animals play a role in the interpretation and assessment of toxicology studies. A brief primer will be offered on current regulatory guidance, in addition to highlighting complex issues that are frequently faced when reviewing applications for biopharmaceuticals. Examples from US Food and Drug Administration submissions will be discussed to illustrate these challenges and to present scientific and regulatory strategies that have been used in the design or review of nonclinical programs that support biopharmaceutical drug development. This course will provide an understanding of the considerations of key issues for advancing these therapeutics safely in the clinic. This requires a strong understanding of the biology of the target and also a good comprehension of the caveats and limits of the current nonclinical models and an ability to design fit-for-purpose, creative, nonclinical safety testing funnels adapted to the test agents being developed.

It's Not Smoke and Mirrors: Demystifying Nonclinical Development Strategies for Biotherapeutics. Jorg Blumel, Genentech, South San Francisco, CA.

Relevant Species Selection: Is It as Easy as Pulling a Rabbit Out of a Hat? Maggie Dempster, GlaxoSmithKline, King of Prussia, PA.

Managing Immunogenicity: Now You See It and Now You Don't. Robert Caldwell, AbbVie, Worcester, MA.

The Final Curtain: Regulatory Insights on the Development of Biotherapeutics; Where Are We Now? Christopher Ellis, US FDA Center for Drug Evaluation and Research, Silver Spring, MD.

In Vitro Testing: Tales from the Real World

Sunday, March 11, 8:15 AM to 12:00 Noon
AM06 | MORNING COURSE

Chairperson(s): *Kelly Coleman, Medtronic PRL, Minneapolis, MN; and Amy Clippinger, PETA International Science Consortium Ltd., Norfolk, VA.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

Other Endorser(s):
Medical Device and Combination Product Specialty Section
Regulatory and Safety Evaluation Specialty Section

Advances in science and technology have paved the way for a paradigm shift in toxicity testing. We now have the opportunity to more efficiently evaluate substances and better protect human health and the environment by using approaches grounded in human mechanisms rather than animals. Acute toxicity tests—namely, skin and eye irritation, skin sensitization, and systemic (oral, dermal, and inhalation) toxicity—are commonly conducted on medical devices, pesticides, industrial chemicals, pharmaceuticals, cosmetics, and other substances. Thus, it is important to implement rigorous alternative acute toxicity-testing approaches that will protect human health and the environment while reducing the time, cost, and animal use associated with traditional toxicity testing. The goal of this course is to teach attendees about existing *in vitro*, *in chemico*, and *in silico* acute toxicity tests and how they have been successfully applied in integrated approaches to evaluate the toxicity of a wide range of substances. Other approaches, such as the use of waivers or the Globally Harmonized System of Classification and Labeling of Chemicals (GHS) mixtures equation, will be discussed.

The presentations also will highlight the remaining challenges that need to be overcome before alternative methods can be implemented globally and accepted by regulatory agencies. This course will be of interest to toxicologists from diverse sectors, including those from the chemical, pharmaceutical, medical device, and personal care product industries, along with others who want to learn more about currently available non-animal tests and how to use them.

Application of the Reconstructed Human Epidermis (RhE) Model as an *In Vitro* Skin Irritation Test for Detection of Irritant Activity in Medical Device Extracts. Wim de Jong, Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Bilthoven, Netherlands.

Developing, Testing, and Implementing Novel Testing Strategies for Skin Sensitization. Nicole Kleinstreuer, NTP NICEATM, Research Triangle Park, NC.

Replacing Animal Use for Eye Irritation Testing—Once and for All, Let's Get It Done. David Allen, Integrated Laboratory Systems (ILS), Research Triangle Park, NC.

Opportunities to Implement Alternative Approaches in the Crop Protection Sector. Sean Gehen, Dow AgroSciences, Indianapolis, IN.

Moving Toward Implementation: The Role of International Collaboration, Opportunities, and Challenges. Anna Lowit, US EPA, Washington, DC.

Physiologically-Based Pharmacokinetic Modeling to Support Modernized Chemical Safety Assessment

Sunday, March 11, 8:15 AM to 12:00 Noon
AM07 | MORNING COURSE

Chairperson(s): *Miyoung Yoon, ScitoVation, Research Triangle Park, NC; and Alicia Paini, European Commission Joint Research Centre, Ispra, Italy.*

Primary Endorser:
Biological Modeling Specialty Section

Other Endorser(s):
***In Vitro* and Alternative Methods Specialty Section**
Risk Assessment Specialty Section

Physiologically-based pharmacokinetic (PBPK) models have been applied to chemical risk assessment for more than three decades. Extrapolation of animal toxicity findings to humans has been the major application of PBPK models in risk assessment. Under the proposed new toxicity testing paradigm, which relies on data from human-relevant *in vitro* toxicity assays interpreted through computational approaches, PBPK models have been redefined as a critical translation tool for quantitative *in vitro* to *in vivo* extrapolation. The models would link effect concentrations in cell-based assays to equivalent human exposures. PBPK models provide a biologically relevant integration platform to describe the absorption, distribution, metabolism, and excretion of chemicals based on a wide range of *in vitro*, *in silico*, and, if available, *in vivo* information. This course will provide an opportunity to revisit the basic principles of PBPK modeling with a special focus on supporting chemical risk assessment under the new toxicity testing paradigm. In addition to describing the basics of model construction, recent advances in model parametrization, including *in vitro* to *in vivo* extrapolation and *in silico* prediction, will be presented. Evaluation of model performance and reliability along with use of available human data will be discussed. Development and application of the PBPK models

to support risk-based decisions in different tiers of risk assessment will be presented. A hands-on demonstration will be provided, using a free online simulation tool (PLETHEM) to demonstrate the workflow of building and parameterizing a PBPK model, simulating different human populations, and applying the model to translate concentration-effect relationships from cell-based assays or *in vivo* studies to the dose-response relationship in target human populations to support chemical risk assessment. The course will address continuing challenges and future directions in PBPK modeling.

Physiologically-Based Pharmacokinetic Models as a Critical Component in Moving Forward with the New Toxicity Testing Strategies Based on *In Vitro* and Computational Approaches. Alicia Paini, European Commission Joint Research Centre, Ispra, Italy.

Physiologically-Based Pharmacokinetic Models for Risk and Safety Assessment: Basic Principles and Examples of the Applications in Traditional Risk Assessment. Hugh A. Barton, Pfizer, Inc., Groton, CT.

Parameterization of Physiologically-Based Pharmacokinetic Models with Minimum Reliance on *In Vivo* Toxicokinetic Studies: Describing Average Person vs. Population. Lisa M. Sweeney, Naval Medical Research Unit Dayton, Wright Patterson AFB, Dayton, OH.

Examples of the Use of Physiologically-Based Pharmacokinetic Models in Support of *In Vitro* Based Safety Assessment: Hands-On Demonstration of a Work Flow. Miyoung Yoon, ScitoVation, Research Triangle Park, NC.

A Tiered Approach to Incorporate Exposure and Pharmacokinetics Consideration in *In Vitro*-Based Safety Assessment. Cecilia Tan, US EPA, Research Triangle Park, NC.

Approaches for Evaluation of Non-Animal-Based Physiologically-Based Pharmacokinetic Models Including the Use of Human Biomonitoring Data. Jos Bessems, VITO, Mol, Belgium.

Developmental Neurotoxicity Testing: Current Practices and Latest Advancements

Sunday, March 11, 8:15 AM to 12:00 Noon
AM08 | MORNING COURSE

Chairperson(s): *Kristen Ryan, NIEHS, Research Triangle Park, NC; and Susan Makris, US EPA, Washington, DC.*

Primary Endorser:
Neurotoxicology Specialty Section

The potential for neurotoxicity in adults and children remains a high public priority due to concerns that recent increases in the prevalence of neurological disorders may in part be due to chemical effects. Guideline developmental neurotoxicity studies in rodents currently remain the gold standard for risk assessment. However, these studies are triggered tests based on evidence of neurotoxicity in standard adult, reproduction, or developmental studies, and as a result, several thousand compounds with unknown neurotoxic potential are never evaluated. Furthermore, many developmental neurotoxicants are still not captured using the current guidelines due to the lack of specific requirements in the guidelines, the subjective nature of these tests causing interlaboratory variability, lack of relevance of some of the assays to human-specific outcomes, and the lack of power to capture subtle deficits. To address some of these issues, concerted efforts have been made in the recent past to advance the science for developmental neurotoxicity testing and to recommend strategies for harmonizing guideline studies for use by regulatory agencies. This course is designed to highlight the current state of the science and recent advancements to identify an integrated strategy for developmental neurotoxicity testing. The course will begin with an introductory talk on the overall practices with current guideline toxicology studies, as well as developments and recommendations for them (US Environmental Protection Agency (US EPA) 870.6300, Organisation for Economic Co-operation and Development (OECD) 426, OECD 443). The next two speakers will focus specifically on the current practices, advancements, and recommendations in neurobehavioral testing (learning, activity, attention) and neuropathology. The subsequent speaker will then highlight how developmental neurotoxicity is assessed in the clinic, provide case examples, and speak on the parallels between human and rodent studies. The last speaker will describe a novel strategy to rapidly screen for compounds with unknown neurotoxic potential to prioritize for further testing and how to incorporate triggers from those screens in further assessment of *in vivo* developmental neurotoxicity studies.

Introduction and Course Goals. Kristen Ryan, NIEHS, Research Triangle Park, NC.

Introduction to Developmental Neurotoxicity Testing—History, Guidelines, Use in Risk Assessment, and Current Recommendations. Susan Makris, US EPA, Washington, DC.

Assessment of Neurobehavior in Developmental Neurotoxicity Rodent Studies. Larry Sheets, Bayer CropScience, Research Triangle Park, NC.

Histopathology and Morphometry Assessments in Developmental Neurotoxicity Testing. Catherine Picut, Charles River Laboratories International, Inc., Durham, NC.

Tools and Strategies for Assessing Developmental Neurotoxicity in Clinical Research. Kimberly Yolton, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

Advancing Developmental Neurotoxicity Testing in the 21st Century: A Potpourri of *In Vitro* and Guideline Studies. Mamta Behl, NIEHS, Research Triangle Park, NC.

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Consumer Products Safety Assessment: Progress in the Use of Alternatives to Animal Models

Sunday, March 11, 1:15 PM to 5:00 PM
PM09 | AFTERNOON COURSE

Chairperson(s): *Kathryn E. Page, The Clorox Company, Pleasanton, CA; and Thomas Hartung, Johns Hopkins Center for Alternatives to Animal Testing (CAAT), Baltimore, MD.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

Other Endorser(s):
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

To meet consumer preferences and changes in the regulatory landscape, the use of animals for the safety evaluation of consumer product ingredients and formulas has largely been phased out by cosmetics manufacturers, and other consumer products companies are soon to follow. The purpose of this course is to provide an encompassing overview of the progress in the field of safety evaluation of consumer products ingredients using alternative approaches. The introductory presentation will map the current landscape of alternative methods for assessing consumer product safety, including highlighting the holes still remaining in the field. Occasional resistance to change by regulatory agencies can be frustrating to the industry at large. However, recent government-industry collaboration has shown the potential for helping the process progress. The first presentation will provide insight into the current regulatory landscape of the US Consumer Product Safety Commission (CPSC) animal testing policy, including what methods are approved and recommended, as well as the struggles faced to get there. A roadmap of where testing and regulations are likely headed also will be presented, including what challenges await. Several alternative methods have been developed and validated to assess product safety and are now considered acceptable by regulatory agencies. However, the path to their integration into safety assessments and communication to scientists-at-large is still a work in progress. The second presentation will showcase available options for alternative testing strategies, as well as struggles and triumphs in getting methods accepted by regulatory agencies. The final two presentations will provide case studies of how alternative testing is used in the cosmetics and cleaning products industries, as well as specific examples from L'Oreal as a trendsetter in the field and regarding method development and from Clorox about how to navigate the current regulatory requirements for cleaning products and animal testing. The course will provide a sound understanding of the current and proposed future state of alternatives to animal testing in consumer products safety assessment.

Embracing New Approaches: A Challenging, but Rewarding, Endeavor. Thomas Hartung, Johns Hopkins Center for Alternatives to Animal Testing (CAAT), Baltimore, MD.

The Regulatory Perspective: Approaches for Development, Validation, and Utilization of Alternative Methods for Toxicity Testing. Joanna Matheson, US Consumer Product Safety Commission, Rockville, MD.

Alternative Methods: The How, the Now, and the Future. Allison Hilberer, Institute for In Vitro Sciences, Inc., Gaithersburg, MD.

Cosmetics: A Case Study. Kristin Yamada, L'Oreal, Clark, NJ.

Cleaning Products: A Case Study. Kathryn E. Page, The Clorox Company, Pleasanton, CA.

Evaluation of Leachable Substances from Materials with Applications in Foods and Pharmaceuticals: Science- and Risk-Based Approaches

Sunday, March 11, 1:15 PM to 5:00 PM
PM10 | AFTERNOON COURSE

Chairperson(s): *Greg L. Erexson, AbbVie, North Chicago, IL; and Kim L. Li, Amgen Inc., Thousand Oaks, CA.*

Primary Endorser:
Medical Device and Combination Product Specialty Section

Other Endorser(s):
Risk Assessment Specialty Section

Polymeric materials commonly used in food and pharmaceutical manufacturing and packaging components are known to leach chemical substances into the final products. The leachable substances may present potential safety risks to consumers and patients. The goal of this course will be to provide an overview of scientific and technical considerations relevant to the assessment of leachable substances covering historical and current context on patient safety and product quality, collaboration between chemists and toxicologists, best practices for deriving chemical-specific safety limits, and use of *in silico* QSAR tools to advance the 3R principle to replace, reduce, and refine animal testing. This course will provide a comprehensive overview of the risk assessment process for leachable compounds from food contact and pharmaceutical materials.

Evaluation of Leachable Substances from Materials with Applications in Foods and Pharmaceuticals: Science- and Risk-Based Approaches. Kim L. Li, Amgen Inc., Thousand Oaks, CA.

Extractables and Leachables Assessment for Patient Safety and Product Quality: Background and Current Context. Greg L. Erexson, AbbVie, North Chicago, IL.

Chemical Characterization of Packaging and Delivery Systems. Cheryl M. Stults, C&M Consulting, LLC, San Mateo, CA.

Safety Evaluation of Leachables/Extractables. Thomas Broschard, Merck KGaA, Darmstadt, Germany.

Use of Computational Approaches to Assess the Toxicity of Extractable and Leachable Substances. Ron Brown, US FDA, Silver Spring, MD.

CE Books Available Exclusively in Electronic Format

Course registrants will receive information on accessing the electronic CE course book prior to the meeting and/or may pick up a USB drive containing a copy of the electronic book on-site.

Lead Optimization of Therapeutic Small Molecules: From Drug Target to Clinical Candidate Selection—Strategies and Decision Making

Sunday, March 11, 1:15 PM to 5:00 PM
PM11 | AFTERNOON COURSE

Chairperson(s): *Dolo Diaz, Denali Therapeutics Inc., South San Francisco, CA; and Dinah Misner, Alios Biopharma, South San Francisco, CA.*

Primary Endorser:
Drug Discovery Toxicology Specialty Section

Other Endorser(s):
Cardiovascular Toxicology Specialty Section
***In Vitro* and Alternative Methods Specialty Section**

From the decision to drug a chosen target with a small or large molecule to the selection of a lead candidate to take into Good Laboratory Practices (GLP) toxicology studies, discovery toxicologists engage an arsenal of tools and strategies with the objective of selecting molecules with a safety profile that provides an optimal chance of clinical success. This is best achieved by early safety involvement in target selection and target de-risking, selection of the best possible chemical matter with minimal off-target effects through lead optimization, and robust safety characterization and investigation of safety issues as they arise. The premise is that robust and thoughtful early safety involvement would reduce attrition in later phases of drug development. This course will provide a comprehensive overview of the strategies and approaches leading from drug target selection to lead identification, optimization, and selection of clinical candidates for first-in-human studies. The first presentation will address the safety considerations in target selection, to ensure that the intended targets are tractable from a safety perspective, and that the relevant questions are addressed and the proper lead optimization paradigms are in place for a particular program. The second presentation will tackle the critical aspects of selectivity for small molecules, including related and unrelated off-targets, and how to ensure that the molecules that are progressed are screened appropriately to ultimately have minimal off-target effects. The next two presentations will focus on two essential aspects of lead optimization: 1) cardiovascular safety and 2) genotoxicity, for which *in vitro* models have been particularly effective in minimizing liabilities. The session will continue with a presentation focused on particularly promising *in vitro* models and strategies to minimize hepatotoxicity; these approaches are becoming increasingly important in drug discovery since preclinical *in vivo* studies poorly identify human-relevant hepatotoxicants. The course will conclude with a presentation that integrates the different aspects of lead optimization discussed previously with *in vivo* data generated in pilot toxicity studies and will discuss how to incorporate these data into deciding whether to move into GLP toxicology studies. All presentations will focus on the practical aspects of implementing thoughtful de-risking strategies and on how data-driven decisions are made with the data outputs; presenters also will provide relevant examples to illustrate these approaches. The course will provide understanding of how to address safety for small molecules from the inception of a program to candidate selection into investigational new drug (IND)-enabling studies, how to evaluate and integrate relevant data, and how to make good decisions related to compound progression.

Target Safety Assessments: How to Lay the Safety Foundation for a Successful Small Molecule Drug Discovery Program. Rebecca Erickson, Denali Therapeutics Inc., South San Francisco, CA.

Lead Optimization to Increase Selectivity and Minimize Off-Target Effects. Yu (Zoe) Zhong, Genentech, Inc., South San Francisco, CA.

Strategies for Assessment of Cardiovascular Safety during Lead Optimization: How to Avoid Human Safety Risks While Not Throwing Out Babies with the Bathwater. Derek Leishman, Eli Lilly and Company, Indianapolis, IN.

Early Mechanistic Genetic Toxicology Screening: Strategies from Chemical Series to Compound Selection Prevent Late-Stage Attrition of Drug Development Candidates. Maik Schuler, Pfizer, Inc., Groton, CT.

Assessing Hepatotoxicity Risk in Drug Discovery: Practical Strategies and Decision Making. William Proctor, Genentech, Inc., South San Francisco, CA.

Lead Optimization Strategies and Integrated Assessment of *In Vitro* and *In Vivo* Toxicology Studies for the Rapid Identification of Clinical Candidates. Mark Fielden, Amgen Inc., Thousand Oaks, CA.

NGS-Based Technologies Enable Biomarker Development and Discovery in Toxicology

Sunday, March 11, 1:15 PM to 5:00 PM
PM12 | AFTERNOON COURSE

Chairperson(s): *B. Alex Merrick, NIEHS, Research Triangle Park, NC; and Andrew B. Nixon, Duke University Medical Center, Durham, NC.*

Primary Endorser:
Biotechnology Specialty Section

Other Endorser(s):
Drug Discovery Toxicology Specialty Section
Molecular and Systems Biology Specialty Section

Next-Generation Sequencing (NGS) represents a series of powerful platforms that have revolutionized DNA and RNA analysis. The simultaneous sequencing of millions of DNA molecules can rapidly provide mechanistic insights into toxicology and biomarker discovery. Evolution of NGS technologies has improved the overall sensitivity and accuracy of these sequencing platforms, allowing for the development of new biomarker assays from tissue, blood, and other biofluids. NGS technologies can identify potential molecular indicators at the cellular and toxicopathological level in response to xenobiotics. The goal of this course is to review NGS-based technologies, demonstrate how they can be used as tools for target discovery in tissue and blood, and suggest best practices for optimal sample acquisition and processing in the toxicology setting. The technological transition from microarray toward NGS platforms in toxicology will be briefly reviewed. In the first presentation, a broad overview will be provided on the development, validation, and implementation of circulating biomarkers from a clinical perspective. Emphasizing lessons learned from the clinical oncology field, where biomarker development is key to disease treatment, the implementation of NGS and its potential use in toxicology will be discussed. The second presentation will describe the roles of non-coding RNAs as potential biomarkers. RNA-Seq data will be presented on long-noncoding RNAs (lncRNAs), recognized as key regulators and potential biomarkers of toxicological responses in humans

and animal models. lncRNAs are an exciting and emerging area in toxicology. The third presenter will focus on another type of noncoding RNA, microRNAs (miRNAs), which are small ~22nt RNAs and represent promising new biomarkers; the isolation, NGS analysis, specific cell and tissue localization, and toxicologic responses *in vitro* in tissues and biofluids will be discussed. The fourth presentation will highlight best practices for optimal sample collection to ensure success with downstream NGS applications, followed by an introduction to whole exome sequencing (WES) in toxicology. WES enriches coding regions of the genome to discover mutations and sequence variants. A new WES platform, which is designed for rats, with future directions toward analysis of circulating, cell-free DNA (ccfDNA) as a potential biomarker for targeting specific biological processes, such as inflammation, will be described. The final presentation will involve NGS methods in epigenetics, using whole-genome bisulfite sequencing (WGBS), as well as other approaches to assess changes in DNA methylation after chemical exposure. Case studies will include the valuable role of zebrafish as an alternative animal model in chemical toxicity screening for NGS-based environmental epigenetics. This course will be of broad interest to investigators in academia, pharma, and government wishing to explore and expand their interest in novel NGS-based approaches with an emphasis on the development and discovery of biomarkers for the detection of xenobiotic toxicity and exposure.

Next-Generation Sequencing Platforms in Toxicology.
Bruce A. Merrick, NIEHS, Research Triangle Park, NC.

Biomarker Development and Application to Toxicology.
Andrew B. Nixon, Duke University Medical Center, Durham, NC.

Understanding the Regulation of lncRNAs during Toxicological Response Using RNA-Seq. Julia Yue Cui, University of Washington, Seattle, WA.

Next-Generation-Sequencing Applications for MicroRNA Biomarker Discovery in Toxicological Studies. Brian N. Chorley, US EPA, Research Triangle Park, NC.

Whole Exome Sequencing in Toxicology: Principles, Tissue Handling, and a New Rat WES Platform. Julie F. Foley, NIEHS, Research Triangle Park, NC.

Leveraging Illumina-Based Sequencing to Reveal Chemically-Induced Alterations in Genome-Wide Cytosine Methylation. David C. Volz, University of California Riverside, Riverside, CA.

Uncertainty Characterization in 21st-Century Toxicology: Current Practice and Practical Methods Supporting Regulatory Risk Assessment

Sunday, March 11, 1:15 PM to 5:00 PM
PM13 | AFTERNOON COURSE

Chairperson(s): *Kristi Muldoon-Jacobs, US Pharmacopeial Convention, Rockville, MD; and Andrea Richarz, European Commission Joint Research Centre, Ispra, Italy.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

Other Endorser(s):
Biological Modeling Specialty Section
Regulatory and Safety Evaluation Specialty Section

Understanding, describing, and, if possible, quantifying uncertainties is an essential part of risk assessment which needs to be communicated clearly to risk managers to support informed decision making. It requires a transparent statement of the likelihood of possible outcomes as a basis of building confidence in decisions taken. This is particularly true for risk assessments that rely on new toxicological methods with which the risk assessment community does not have the benefit of historical experience. The course will clarify the nature and sources of uncertainties and variability and give an overview of existing initiatives and available guidance for uncertainty evaluation for chemical risk assessment in the regulatory context. Current practice in regulatory review will be discussed, as well as challenges in application for the risk assessor/manager (often the same person) in industry. The importance and challenges of communicating uncertainties also will be addressed. A special focus of the course will be the characterization of uncertainties for alternative methods used for chemical hazard and risk assessment, bearing in mind that the incorporation of new toxicological methods into risk assessment is still hampered by lack of knowledge on how to describe and assess the associated different uncertainties. The new methods, for example, combine *in silico*, *in vitro*, and high-throughput toxicokinetics approaches to predict hazards and to provide quantitative estimates of effect levels and are then combined into models to predict *in vivo* effect levels, such as lowest-observed-adverse-effect levels (LOAELs). Approaches will be shown to quantify uncertainty in these individual inputs, as well as methods to combine uncertainty across all inputs in the final models. Furthermore, uncertainty and variability are

compared with those in the *in vivo* databases that are used as benchmarks for the new models. Another example will include consideration of uncertainties for the non-chemical-specific Threshold of Toxicological Concern (TTC) approach as compared to traditional hazard assessment. The course will further describe state-of-the-art mathematical, statistical, and other methods, such as expert elicitation, to characterize and quantify uncertainty and tiered approaches to handling uncertainty in risk assessment. Examples will illustrate qualitative, deterministic, and probabilistic uncertainty assessment. Two case studies will show how these methods can help risk assessors and support decision making: 1) the use of Bayesian-belief networks to quantify the uncertainty in the potential of a chemical being a skin sensitizer in the light of competing evidence and 2) a mathematical model for an adverse outcome pathway (AOP)-based risk assessment, defined and parameterized using *in vitro* data sources. Overall, the purpose of the course is to give an overview of the concept of uncertainty and to identify existing resources on uncertainty characterization and reporting in guidance related to hazard assessment, as well as available mathematical methods. Practical examples based on experience from practice in various sectors will emphasize alternative methods supporting hazard assessment. Thus, the course will present concrete methods to characterize uncertainty in the context of chemical risk assessment, in particular how to pragmatically apply them in a tiered approach, while gaining more confidence in assessing alternative methods.

Introduction to Uncertainty: Definitions and Importance for Risk Assessment. Kristi Muldoon-Jacobs, US Pharmacopeial Convention, Rockville, MD.

Considerations of Uncertainty Assessment in Existing Guidance Documents Linked to Chemical Safety Assessment and Current Regulatory Practice. Andrea Richarz, European Commission Joint Research Centre, Ispra, Italy.

Challenges and Opportunities in the Application and Communication of Uncertainty Assessment. Heli M. Hollnagel, Dow Europe GmbH, Horgen, Switzerland.

Using Mathematics to Characterize Uncertainty with Examples from Alternative Approaches in Toxicological Risk Assessments. John Paul Gosling, University of Leeds, Leeds, United Kingdom.

Characterization of Uncertainty in *In Silico*, *In Vitro* Assay, and High-Throughput Toxicokinetics Data and Their Combination and Comparison with *In Vivo* Data Uncertainties. Richard Judson, US EPA, Research Triangle Park, NC.

CE Books Available Exclusively in Electronic Format

Course registrants will receive information on accessing the electronic CE course book prior to the meeting and/or may pick up a USB drive containing a copy of the electronic book on-site.

Xenobiotic Pharmacokinetics during Pregnancy and Lactation

Sunday, March 11, 1:15 PM to 5:00 PM
PM14 | AFTERNOON COURSE

Chairperson(s): *Natasha Catlin, Pfizer, Inc., Groton, CT; and Angela Slitt, University of Rhode Island, Kingston, RI.*

Primary Endorser:
Reproductive and Developmental Toxicology Specialty Section

Other Endorser(s):
Mechanisms Specialty Section
Risk Assessment Specialty Section

Exposure to xenobiotics during pregnancy and lactation is unavoidable and can be either intentional with pharmaceuticals or unintentional as contaminants in air, food, and water. During this critical time period of development, xenobiotic exposure can result in deleterious effects to the developing fetus. A number of critical physiological and molecular changes occur in the pregnant woman or animal that will influence the disposition and toxicity of chemicals, often in a gestational age-dependent manner. These changes range from altered blood flow to changes in metabolic pathways, as well as enhancement of renal filtration. In addition, the placenta is considered a selective barrier to protect the fetus against xenobiotics. However, some pharmaceuticals and toxicants can readily cross this placental barrier through active transport or diffusion, leading to exposure *in utero*. After birth, lactation represents a new route of xenobiotic exposure for the infant. The goal of this course is to provide participants with an introduction to the maternal and perinatal pharmacokinetics of xenobiotics during pregnancy and lactation. A variety of approaches will be covered, including animal studies, physiologically-based pharmacokinetic (PBPK) modeling, and clinical pharmacology studies in pregnant women. Case study examples also will be discussed in each presentation to illustrate these different approaches. The first presentation will provide an overview of the maternal physiologic changes associated with pregnancy, as well as the metabolic capabilities of fetal and neonatal rodents and humans. The second lecture will discuss placental morphology and the transfer of nutrients and foreign chemicals. The third presentation will cover the application of PBPK modelling to understand how physiological and biochemical processes impact tissue dosimetry of xenobiotics during gestation, fetal, and early-life stage development. The final presentation will describe clinical pharmacology examples of pharmacokinetic changes during pregnancy and the postpartum period and will provide an overview of xenobiotic transfer through breast milk. This course also will cover changes in pharmaceutical drug labeling related to pharmacokinetics and pharmacology during pregnancy and lactation.

Overview of Maternal and Fetal Physiology and Pharmacokinetics. Jamie Moscovitz, Pfizer, Inc., Boston, MA.

Life-Stage Physiologically-Based Pharmacokinetic (PBPK) Models in Humans and Animals. Hisham El-Masri, US EPA, Durham, NC.

Disposition and Toxicity of Xenobiotics in the Placenta throughout Pregnancy. Richard Miller, University of Rochester, Rochester, NY.

Clinical Implications of Pharmacokinetic Changes during Pregnancy and Lactation. Mary Hébert, University of Washington, Seattle, WA.

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Scientific Sessions

Opening Plenary Lecture

Developing Genome-Edited Stem Cells for Therapy of Patients: Assessing Efficacy and Toxicology

Monday, March 12, 8:00 AM to 9:00 AM

Lecturer: *Matthew H. Porteus, Stanford University, Stanford, CA.*

Genome editing provides a mechanism to precisely alter the DNA sequence of a cell. The most efficient mechanism to achieve genome editing is to induce a site-specific DNA double-strand break at the genomic target site to be modified, thereby activating the cell's own repair machinery. The CRISPR-Cas9-gRNA system has accelerated the field of genome editing because of its ease of use, its high on-target activity, and its high specificity compared to other nuclease platforms. If a donor template is provided along with the nuclease, the cell will use that donor template to repair the break by homologous recombination and precise sequence changes can be introduced into the target gene. We have focused our efforts on developing a clinically compatible method of engineering human primary blood cells, including hematopoietic stem cells, by homologous recombination. Using this system, we now achieve gene editing by homologous recombination frequencies of 40–80% in CD34+ hematopoietic stem and progenitor cells and 20–50% in primary human T cells. I will discuss our translation of this process to the clinic for genetic diseases of the blood and immune system, including sickle cell disease, and our ability to use homologous recombination to engineer complex phenotypes in primary human T cells.

As genome-edited primary human cells are a novel therapeutic, a careful assessment of the safety and toxicology of such products is critical. Traditional methods of evaluating such toxicology using the paradigms of small molecules or biologics may not be appropriate for this different class of therapeutics. Genetically engineered cell based therapeutics have a different PK/PD profile, for example, that needs to be considered. I will discuss some of the approaches we have taken to evaluate safety and toxicology in our genome-edited cell based products.

Plenary Keynote Medical Research Council (MRC) Lecture

Circadian Clocks: Setting the Tempo of Our Life

Wednesday, March 14, 12:30 PM to 1:30 PM

Lecturer: *Michael Hastings, MRC Laboratory of Molecular Biology, Cambridge, United Kingdom.*

Circadian (approximately one day) rhythms dominate our lives, most obviously via the sleep/wake cycle. Driven by internal clocks, they adapt us to the world by preparing tissues to perform appropriate, but very different, functions in anticipated day and anticipated night. The suprachiasmatic nucleus (SCN) of the hypothalamus is the principal circadian clock of the mammalian brain. It is entrained to solar time by direct retinal innervation, and in turn, it co-ordinates innumerable cellular clocks distributed in all major organs across the body. At a cellular level, circadian timekeeping in SCN and other cells pivots around self-sustaining transcriptional/translational feedback loops (TTFLs) in which the positive regulators CLOCK and BMAL1 drive expression of the negative regulators PERIOD (PER) and CRYPTOCHROME (CRY) via E-box DNA regulatory sequences. Delayed negative feedback by PER and CRY at E-boxes, followed by degradation of PER and CRY, establishes a spontaneous oscillation with a period of approximately 24 hours. This mechanism orchestrates local cell type-specific circadian transcriptomes, synchronized by SCN-dependent behavioral, neuroendocrine, and autonomic cues. These programs in turn sustain the coherent 24-hour cycles of local gene expression that underpin circadian behavior, metabolism, and physiology. This presentation will review recent advances in understanding of the molecular genetic basis of the cell-autonomous clock mechanism of the SCN. It will then consider how circuit-level cellular interactions establish the SCN as a powerful self-sustained clock. Finally, it will consider how the SCN directs circadian behavior and physiology. Where appropriate, it will illustrate how developments in real-time imaging of neuronal function and genetic code expansion have been useful in elucidating the clock's inner mechanism. The overarching message from the circadian neurobiology field is that our bodies are extremely sophisticated 24-hour machines, an observation with significant implications for health and disease.

SOT/EUROTOX Debate

Adverse Outcome Pathways Are the Future for Regulatory Toxicology

Monday, March 12, 4:45 PM to 6:00 PM

Chairperson(s): *Ron Hines, US EPA, Research Triangle Park, NC; and Heather Wallace, University of Aberdeen, Aberdeen, United Kingdom.*

SOT Debater: *Daniel Villeneuve, US EPA, Duluth, MN.*

EUROTOX Debater: *Brigitte Landesmann, European Commission Joint Research Centre Institute for Health and Consumer Protection, Ispra, Italy.*

Endorser(s):
Society of Toxicology (SOT)
European Societies of Toxicology (EUROTOX)

Each year, the SOT Annual Meeting includes a debate in which leading toxicologists advocate opposing sides of an issue of significant toxicological importance. The debate continues a tradition that originated in the early 1990s. This year, the debaters will address the the proposition "Adverse Outcome Pathways Are the Future for Regulatory Toxicology."

Following the recommendations of the 1997 National Academy of Sciences Report *Toxicity Testing in the 21st Century, A Vision and Strategy*, there has been considerable effort in identifying and characterizing toxicity pathways, i.e., biological pathways with which environmental stressors interact, resulting in an adverse outcome. The toxicity pathway concept was expanded from a focus on individual, human toxicity to adverse impacts on populations and ecosystems with the landmark paper by Ankley et al. (*Environ Toxicol Chem* 29:730–740, 2010) in which the term adverse outcome pathway (AOP) was coined and defined as "a [chemically agnostic] conceptual construct that portrays existing knowledge concerning the linkage between a direct molecular initiating event and an adverse outcome at a biological level of organization relevant to risk assessment." Since that time, there have been numerous workshops and studies expanding and refining the AOP framework such that it now encompasses signaling networks and represents a framework for organizing and presenting data gathered using multiple approaches. In a joint effort between the US Environmental Protection Agency (US EPA) and Organisation for Economic Co-operation and Development (OECD), an AOP knowledge base is being developed. Although the AOP framework has seen widespread acceptance within the environmental sciences, the use of the framework as a risk assessment and decision-making tool is less apparent. The debaters will discuss the state of the AOP science and whether the AOP concept is simply a research tool or truly represents a framework that will serve as the basis for most future regulatory decision making.

Regardless of framework differences and personal convictions, each scientific debate delegate will present relevant evidence and compelling scientific arguments to persuade and appeal to the audience in order to obtain the approval or refusal of the motion. In addition to being a featured session at this meeting, this debate will again take place (with the debaters taking the reverse positions) in Brussels, Belgium, during the 54th Congress of the European Societies of Toxicology (2018 EUROTOX Annual Congress), September 2–5, 2018.

Meet the Directors

A Conversation with Linda S. Birnbaum, Mark S. Johnson, and Edward J. Perkins

Tuesday, March 13, 11:00 AM to 12:00 Noon

Chairperson(s): *Leigh Ann Burns Naas, Gilead Sciences, Inc., Foster City, CA.*

Panelists: *Linda S. Birnbaum, NIEHS, Research Triangle Park, NC; Mark S. Johnson, US Army Public Health Center, Aberdeen Proving Ground, MD; and Edward J. Perkins, US Army Engineer Research and Development Center, Vicksburg, MS.*

This important session will provide an informal venue for meeting attendees to have a candid and open discussion with three key leaders of federal organizations with missions to protect and improve public health: Linda S. Birnbaum, PhD, DABT, ATS, director, National Institute of Environmental Health Sciences (NIEHS), and Mark S. Johnson, PhD, DABT, ATS, and Edward J. Perkins, PhD, two directors from the US Department of Defense (US DoD). The entire session will be devoted to a question-and-answer format concerning scientific directions and priorities for NIEHS and US DoD (e.g., DTRA, DARPA, SERDP, and ESTCP), including funding priorities and outlooks and training opportunities. Dr. Birnbaum has served as the director of the National Institute of Environmental Health Sciences and the National Toxicology Program since 2009. Dr. Johnson is the director of toxicology at the US Army Public Health Center and the chair of the Tri-Service Toxicology Consortium. Dr. Perkins is a senior scientist in environmental networks and toxicology at the US Army Engineer Research and Development Center.

Society of Toxicology and Japanese Society of Toxicology Symposium

Environmental Neurodevelopmental Risk

Wednesday, March 14, 8:00 AM to 10:45 AM

Chairperson(s): *Leigh Ann Burns Naas, Gilead Sciences, Inc., Foster City, CA; and Jun Kanno, Japan Organization of Occupational Health and Safety, Kanagawa, Japan.*

The Society of Toxicology (SOT) and the Japanese Society of Toxicology (JSOT) are delighted to jointly sponsor a symposium on a topic of mutual interest: environmental neurodevelopmental risk. Each Society has selected from among its membership leaders in the field to provide their perspectives on recent advances in this area. Understanding critical organ system developmental windows is crucial for determining potentially unique susceptibility to chemical exposure. In 2000, a workshop aimed at identifying how chemical exposure timing during the pre-conception, prenatal, and postnatal period affects outcomes did much to bring to light the concern for potential health risk to these life stages with respect to multiple organ systems, including the central nervous system. In the intervening years, substantial research efforts and regulatory discussion has occurred to identify agents which may impact these systems in a negative way in additional critical developmental phases. Notably, with respect to the developing brain, a significant and controversial debate has arisen across the public domain regarding the notable rise in neurodevelopmental disorders (e.g., attention deficit hyperactivity disorder (ADHD), autism/autism spectrum, learning disabilities, etc.) observed in children over the past 10+ years. While some of the increase (typically cited as a 10–20% rise over the past decade) can be attributed to changes in diagnostic criteria and reporting methodologies, there is still up to 40% of this increase which does not have an identifiable cause. The etiology of neurodevelopmental disorders is clearly a complex and multifactorial one. Genetics may play a role, but alone do not account for the rise in incidence. It is clear that many chemicals can interfere with brain development, some at very low systemic exposures. When this exposure occurs during specific critical developmental windows, the potential for lasting and/or heritable (epigenetic) effects exists. This symposium will explore evidence that exposure to a variety of environmental chemicals at different stages of neurological development may play unique roles in neurodevelopmental risk and will discuss possible paths forward to help curb the rise in this effect in future generations.

Adverse Effects of Neonicotinoids on Mammalian Brain Development: Possible Risk Factors for Neurodevelopmental Disorders Like Autism or ADHD?

Lecturer: *Yoichiro Kuroda, Environmental Neuroscience Information Center, Tokyo, Japan.*

Junko Kimura-Kuroda, Tokyo Metropolitan Institute of Medical Science is a co-author of this research. In the United States, Republic of Korea, and Japan, incidence of neurodevelopmental disorders, such as autism and attention deficit hyperactivity disorder (ADHD), has been increased in recent decades. The cause of increase is obviously not genetic, but environmental. Genetic background (more than 800 autism-related genes have been reported) concerning synaptogenesis for higher functions in such impaired children's brain contributes vulnerability of the disorders. Many environmental chemicals trigger the developmental disorders. Epidemiologic and animal studies demonstrate associations between exposure to organophosphate pesticides and neurodevelopmental disorders, such as decreased cognitive function and behavioral problems. Perinatal exposures of various environmental chemicals (pesticides, PCBs, methylmercury, etc.) disrupt gene expression for synaptogenesis spatiotemporally. Neonicotinoids are used worldwide as pesticides, and with similar chemical structures to nicotine, neonicotinoids also share agonist activity at nicotinic acetylcholine receptors (nAChRs). Because of the importance of nAChRs for mammalian brain development, adverse effects of neonicotinoid exposure in fetus and children are concerning. Previously, we showed that nicotine and two neonicotinoids, acetamiprid and imidacloprid, exert similar excitatory effects on rat cerebellar neurons. Furthermore, we reported these neonicotinoids disrupt expression of synaptogenesis-related genes in rat developing cerebellar cultures, by whole genome microarray. Other reports demonstrate that maternal exposure of neonicotinoids induced behavioral problems in her pups' mice. Neonicotinoids disrupt human α4β2 and α7 nAChRs responses against the endogenous ligand acetylcholine. These data suggest neonicotinoids are possible causal factors of neurodevelopmental disorders.

The Impact of Prenatal Exposure to Phenols and Phthalates on Early Cognitive Development

Lecturer: *Susan L. Schantz, University of Illinois at Urbana-Champaign, Urbana, IL.*

The potential for exposure to endocrine-disrupting chemicals (EDCs), including phthalates, bisphenol A (BPA), and recent replacements for these chemicals, to affect neurodevelopment is of growing concern. Exposure to these chemicals occurs through a wide range of consumer products and is ubiquitous among pregnant women. Prenatal exposure to phthalates and BPA has been associated with adverse neurodevelopmental outcomes during childhood. However, few, if any, studies have assessed the effects of these chemicals or their replacements on cognitive development during infancy. In an effort to characterize more specific aspects of cognition and obtain results earlier in life than most previous studies, our research group is using innovative measures that are early indicators of later cognitive function. This work builds on research in developmental psychology demonstrating that infant looking behaviors can be used to obtain reliable, stable, and valid measures of basic cognitive processes, including working memory,

information processing speed, and visual attention. Infant looking behaviors also can be used to measure face processing, which is critical for proper social interactions. The Illinois Kids Development Study (I-KIDS) is a prospective pregnancy cohort currently under recruitment at the University of Illinois. I-KIDS has gathered a wealth of information on prenatal exposures and maternal health, diet, demographic, and lifestyle variables, in addition to measuring cognitive outcomes in infants. This talk will describe our approach, which uses infrared eye-tracking to record the infant's looking behavior during the presentation of stimuli and videos on a large-screen high-definition TV. In addition to assessing the impact of prenatal exposures to EDCs, we also will assess whether other maternal risk factors, such as obesity or prenatal stress, interact with chemical exposure to increase risk. Initial results suggesting that both higher maternal prenatal stress and higher maternal prenatal EDC exposure can negatively impact cognitive outcomes in infants will be presented.

Neurobehavioral Toxicity at Adult Period Induced by Neonicotinoid Pesticides Exposure at Juvenile Period of Male Mice

Lecturer: *Satoshi Kitajima, National Institute of Health Sciences, Tokyo, Japan.*

Kentaro Tanemura, Tohoku University, is a co-author of this research. Central nervous system is formed under the genetic information and fine-tuned by the proper neural signals at each developmental phase. The proper neuronal activities are used for the formulation and the maturation of the neural networks, and normal brain functions are established. In this context, the brain dysfunction or morphological defect associated with the behavioral abnormality in the adult phase can be caused by the exogenous disturbance, including chemicals, of neural signals during early periods of brain development.

Under current regulation of chemicals, adult experimental animals are exposed, and the methods to monitor neuronal endpoints are largely limited to those related to peripheral nervous system. Adverse effects on behavioral endpoints are known to be difficult to monitor in such studies. Theoretically, as mentioned above, late neurobehavioral effect induced by early exposure should be addressed by postnatal or perinatal exposure studies. We have developed a screening system to identify delayed neurobehavioral toxicity induced by early exposure to chemicals with quantitative indicators generated by a battery of five tests (i.e., open field test, light-dark transition test, elevated plus maze test, fear conditioned learning test, and prepulse inhibition test). Male C57BL/6 mice were subject to the test battery at the age of 12 weeks (w). Chemical exposure was performed, orally, at 2 w (juvenile exposure, oral gavage) or, for comparison, at 11 w (adult exposure, oral gavage). Here, we report a case study on acetamiprid, a neonicotinoid insecticide. The impairment of learning and memory associated with anxiety-related behavioral anomaly at 12 w were induced by the single oral administration of acetamiprid at 2 w. Immunohistochemical analysis on the brains of 12 w mice revealed reduction in neurogenesis activities in hippocampus. "Percellome" gene expression analysis on the hippocampus of 12 w mice revealed alteration of *gamma*-Aminobutyric acid (GABA) signaling and CREB signaling as a result of juvenile exposure. These findings are considered to link to the behavioral impairments. More details will be presented.

Developmental Exposure to Fine Particle Air Pollution and Neurodevelopmental Disorders

Lecturer: *Deborah A. Cory-Slechta, University of Rochester Medical Center, Rochester, NY.*

Air pollution (a mixture of particles, metals, organic contaminants, and gases) is a worldwide public health problem. Particulate matter (PM) sizes range from coarse (2.5-10 µm) to fine (<2.5 µm) to ultrafine (UFP, <100 nm or 0.1 µm). The UFP component of air pollution is considered most reactive as it provides the greatest surface area for adsorption of toxic organic and metal contaminants. Impacts of air pollution on the brain are increasingly being reported in epidemiological studies. Exposures during the period of early brain development, a period encompassing a highly orchestrated and synchronized trajectory of events, may represent a period of particular vulnerability to such effects and contribute to various neurodevelopmental disorders, likely via inflammatory mechanisms. In a mouse model of gestational exposure to concentrated ambient fine and ultrafine particles, both male and female offspring demonstrated ventriculomegaly, a clinical indicator of poor prognosis for development and cognition. In addition, early and excessive myelination was found which correlated with increased brain iron concentrations in females. Subsequent analyses revealed an accelerated maturation of the oligodendrocyte precursor cells for myelination. Exposures to concentrated ambient UFP during the early postnatal period, considered equivalent to human third trimester associated with rapid neuro- and gliogenesis, produced effects that were more extensive and of greater magnitude in males that included persistent ventriculomegaly, reductions in myelination and size of the corpus callosum, microglial activation, and increases in glutamate. Behavioral changes included impulsivity and learning impairments. Male susceptibility to postnatal exposures may reflect an earlier colonization of brain with activated microglia requisite to neuro- and gliogenesis. Collectively, these findings support a potential role for air pollution in neurodevelopmental disorders. Notably, while neurodevelopmental disorders each have some unique features, they also show extensive overlap in characteristics and are typically heterogeneous in expression. Air pollution, if a risk factor for Alzheimer's disease, could likewise contribute to heterogeneity, given the extensive differences in such exposures in different geographical areas, even within relatively localized areas and in timing of such exposures.

EUROTOX Bo Holmstedt Memorial Award Lecture

Born in the southern part of Sweden in 1918, Bo Holmstedt was an internationally renowned toxicologist. He was known for his outstanding research contributions and his engagement in education and was a leading figure in the toxicology community. In his memory, EUROTOX established the Bo Holmstedt Memorial Lecture. This merit award recognizes scientific excellence in the area of toxicological sciences and is presented to an outstanding European toxicologist at the EUROTOX Annual Congress. For the first time, the SOT Scientific Program Committee is pleased to present a lecture exchange of eminent scientists between SOT and EUROTOX. As part of the exchange, Vera Rogiers, Vrije Universiteit Brussel, (2017 Bo Holmstedt Memorial Lecture awardee) will be presenting at the SOT Annual Meeting, and the 2018 SOT Merit Award recipient Robert J. Kavlock, US Environmental Protection Agency (US EPA), will present at the EUROTOX Annual Congress in Belgium in September 2018.

Human Skin Stem Cell-Derived Hepatic Cells and Their Potential Applications in Toxicology

Wednesday, March 14, 11:00 AM to 12:00 Noon

Lecturer: *Vera Rogiers, Vrije Universiteit Brussel, Brussels, Belgium.*

Human skin-derived precursor cells (hSKP) are somatic, immune-privileged stem cells that reside in the dermis throughout life and harbour a high self-renewal and multipotent capacity. More specifically, it could be shown that besides their ectodermal and mesodermal differentiation potential, they can be directed towards the hepatic lineage. Indeed, upon sequential exposure *in vitro* to hepatogenic growth factors and cytokines, hSKP are able to generate hepatic progenitor-like cells (hSKP-HPC). As such, they represent a convenient human cell source with a normal genotype (patented protocol EP1824965 B1). They express not only hepatic progenitor cell markers, but also some typical features of adult hepatocytes, such as albumin production. They also express a number of key biotransformation enzymes, including CYP1B1, FMO1, GSTA4, and GSTM3, and influx and efflux drug transporters, such as ABCC4, ABCA1, and SLC2A5. These properties give the cells a unique position among the actually existing *in vitro* models, which makes them suitable for pharmaceutical, toxicological, and clinical applications. The predictive capacity of the hSKP-HPC for identifying hepatotoxic compounds was evaluated. Using a toxicogenomics approach, it was found that hSKP-HPC can predict hepatotoxicity equivalent to primary human hepatocytes. They even more closely reflect clinical samples from acute liver failure (ALF) and fatty liver patients in response to hepatotoxic compounds than primary human hepatocytes. The ability of hSKP-HPC to deliver *in vitro* prediction of hepatotoxicity for ALF (acetaminophen), phospholipidosis (amiodarone), and hepatic steatosis (sodium valproate) is especially relevant for drug discovery programs, where drug-induced liver injury (DILI) contributes to high attrition rates. Furthermore, hSKP-HPC's sensitivity to hepatic steatosis underlies its relevance as a disease model for non-alcoholic fatty liver disease (NAFLD), which affects 20% of the adult population and which may evolve into severe, life-threatening non-alcoholic steatohepatitis (NASH). Current preclinical investigations rely on animal or human *in vitro* models that do not accurately reflect clinical NAFLD. We have demonstrated that exposure to steatogenic compounds, including insulin, induces triglyceride accumulation in hSKP-HPC, a central feature of clinical NAFLD. Moreover, it could be shown that the key molecular mechanisms that underlie this effect can be modeled and modulated in hSKP-HPC, providing a valuable disease model for screening of novel anti-NAFLD molecules. Finally, hSKP themselves are key candidates for autologous and allogeneic cell-based therapy for the treatment of liver disease, given their immune privileged state. In a transgenic murine model of liver deficiency (uPA+/+/SCID), injected hSKP cells successfully engrafted survived and repopulated the hepatic liver tissue and contributed to the increase in liver mass. Also, after oral administration of dianabol, an anabolic steroid, the *in vitro*-generated hSKP-derived hepatocytes produced human-specific metabolites, detectable in the urine of the chimeric mice. This clearly demonstrates the *in vivo* biotransformation capacity of the hSKP-derived hepatocytes. Further developments are underway, among which the development of a hSKP-based NASH model suitable for toxicological screening and drug discovery.

Award Lectures

Award lecture titles and descriptions will be available in the Program *and SOT Mobile Event App.*

Distinguished Toxicology Scholar Award Lecture

Monday, March 12, 12:30 PM to 1:30 PM

Lecturer: *Roger O. McClellan, Toxicology & Human Health Risk Analysis, Albuquerque, NM.*

Translational Impact Award Lecture

Tuesday, March 13, 11:00 AM to 12:00 Noon

Lecturer: *Jia-Sheng Wang, University of Georgia, Athens, GA.*

Merit Award Lecture

Tuesday, March 13, 12:30 PM to 1:30 PM

Lecturer: *Robert J. Kavlock, Washington, DC.*

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IAT Advanced Imaging and Microscopy for Retinal Disease and Toxicity

Monday, March 12, 9:15 AM to 12:00 Noon

Chairperson(s): *Melva Rios Blanco, Allergan, Irvine, CA; and Donald Fox, Robson Forensic, Inc., Philadelphia, PA.*

Primary Endorser:
Ocular Toxicology Specialty Section

Other Endorser(s):
Clinical and Translational Toxicology Specialty Section
Neurotoxicology Specialty Section

The three major challenges in the study of acquired and innate diseases, as well as drugs and toxicants that affect the retina in man and experimental animals, are: difficulty in early noninvasive detection of decreased visual function and/or loss with conventional tools and techniques; determination of the cellular site(s) and mechanism(s) of action; and monitoring of progression and/or repair following different treatment/therapeutic regimens. Advances in ocular imaging techniques, for man and experimental animals, provide the ability to noninvasively image individual retinal cells, the optic nerve, and retinal vasculature in living eyes. These new noninvasive techniques enable the clinician and scientist to detect, monitor, and treat retinal disease and injury earlier; to visualize the site of action with greater specificity; and to follow the progress of treatment longitudinally. Moreover, the visualization and determination of the cellular, subcellular, and ultrastructural site and mechanisms of injury in retinas from donated human eyes and experimental animals require a variety of different sophisticated imaging techniques. These newer noninvasive and experimental techniques are readily applicable to the study of drugs and toxicants that produce pathophysiological alterations similar to known retinal and neurodegenerative diseases, or that exacerbate such existing conditions. The objective of the session is to present state-of-the-art research approaches to clinical and experimental animal model imaging and their utility in toxicological research and to show how the obtained data can be utilized for translational research. The presentations will cover the study of different cell populations within the retina and of the supporting vascular networks. Each presentation will share the fundamental aspects of the retina and imaging modalities employed in their work. The first speaker will demonstrate the utility of various optical coherence tomography (OCT) techniques and adaptive optics (AO) to assess morphological and functional changes associated with glaucoma disease progression and treatment in experimental models and evaluation of changes in the retinal nerve fiber layer for early detection. The second speaker will show the utility of AO techniques coupled to advanced imaging techniques to precisely deliver visual stimuli to individual photoreceptors, such that visual function and retinal structure can be studied with cellular resolution in normal and diseased retinas. The third speaker will describe a combination of microscopic techniques from the cellular to ultrastructural to three-dimensional sub-structural levels that elucidate mechanisms of mitochondrial-mediated retinotoxicity in both human and experimental animals. The final speaker will present research focused on the role of hematopoietic stem cells (HSCs) in the physiological and pathological vascular repair in the retina and the utility of imaging and other techniques to study this phenomenon in experimental animals. Overall, the session will accomplish three goals. First, it will introduce and educate the scientific community on the use of state-of-the-art approaches to noninvasive ocular imaging for the early detection, assessment, progression, and treatment of retinal and vascular damage in man and experimental animals. Second, it will enhance the understanding of retinal sites and mechanisms of action of injury. Third, it will provide a basis for determining the translatability of experimental data to humans. The session will be of interest to basic scientists, clinicians, and researchers engaged in drug development and testing.

Introduction. Melva Rios Blanco, Allergan, Irvine, CA.

Cellular and Structural Imaging Techniques in Glaucoma Diagnosis and Treatment. Stuart McKinnon, Duke University, Durham, NC.

Adaptive Optics Imaging to Study Retinal Degeneration and Response to Treatment. Jacque Duncan, University of California San Francisco, San Francisco, CA.

Mitochondria-Mediated Retinotoxicity: Determining Pathophysiological Mechanisms Using Multifaceted Image Analysis and Biochemical Techniques. Donald Fox, Robson Forensic, Inc., Philadelphia, PA.

"Seeing" iPSCs in the Retina during Retinal Repair. Maria Grant, University of Alabama at Birmingham, Birmingham, AL.

Cancer Risk Assessment of PAH Mixtures: Current and Future Directions

Monday, March 12, 9:15 AM to 12:00 Noon

Chairperson(s): *M. Margaret Pratt, US EPA, Washington, DC; and Cynthia Rider, NIEHS, Research Triangle Park, NC.*

Primary Endorser:
Mixtures Specialty Section

Other Endorser(s):
Carcinogenesis Specialty Section

The cancer risk posed by exposures to polycyclic aromatic hydrocarbons (PAHs) has long been a public health concern. The two-year rodent cancer bioassay remains the definitive source of information employed for cancer risk assessment, and using such conventional approaches, the US Environmental Protection Agency (US EPA) is actively working to address the need for an updated and expanded document that serves as the agency's approach for assessing cancer risk from exposure to PAH mixtures. However, the time and resources required to perform two-year rodent bioassays for the range of environmental PAH mixtures are significant and serve as a disincentive to the development of these kinds of data. Recent trends in toxicology and risk assessment offer opportunities to explore less costly and more rapid alternative approaches using non-apical endpoints for estimating the cancer risk posed by PAH mixtures; however, alternative approaches require critical evaluation to ensure that they represent an improvement from the current approach. The approaches that will be discussed in this session include PAH whole mixtures risk assessment, component-based approaches, use of shorter-term *in vitro* and *in vivo* assays to provide cancer-relevant data, and a greater focus on adverse outcome pathways to understand cumulative risk. This will be followed by a panel discussion of the merits of these alternative approaches and

what steps are needed to move toward validation. *Disclaimer: The views expressed are those of the authors and do not necessarily represent the views or policies of the US EPA.*

PAH RPF Mixtures Cancer Risk Estimation: Implementing Peer Review Recommendations. M. Margaret Pratt, US EPA, Washington, DC.

***In Vitro* Screening to *In Vivo* Testing of Polycyclic Aromatic Hydrocarbons at the National Toxicology Program.** Cynthia Rider, NIEHS, Research Triangle Park, NC.

The Genetic Toxicity of Complex Mixtures of Polycyclic Aromatic Hydrocarbons: Evaluating the Dose-Additivity Assumption Using a Transgenic Mouse Model. Paul White, Heath Canada, Ottawa, ON, Canada.

Mechanism-Based Classification of PAH Mixtures to Predict Carcinogenic Potential. Susan Tilton, Oregon State University, Corvallis, OR.

Use of Non-Apical Assay Data in an Integrated Approach to Testing and Assessment of Chemical Mixtures in the Environment: The Advent of Adverse Outcome Pathway Footprinting. Jason Lambert, US EPA, Cincinnati, OH.

Novel Insights on Chemical-Induced Immunotoxicity: Microvesicles and microRNA Dysregulation

Monday, March 12, 9:15 AM to 12:00 Noon

Chairperson(s): *Emanuela Corsini, University of Milan, Milan, Italy; and Stacey Anderson, NIOSH, Morgantown, WV.*

Primary Endorser:
Immunotoxicology Specialty Section

Eukaryotic cells contain extracellular organelles named microvesicles (e.g., exosomes, nanovesicles) that are released into the microenvironment. Microvesicles and their main content microRNAs are believed to play a central role in many physiological and pathological processes, including inflammation, autoimmunity, atherosclerosis, and cancer. miRNAs, a class of non-protein-coding RNA molecules negatively regulating mRNA translation, have been shown to be involved in several cellular processes, and their role in toxicology is emerging. The miRNA-mediated coordinated control of gene expression has been shown to be crucial in immunity, promoting and finely regulating appropriate immune responses. Both microRNA and microvesicles are a very promising tool in identifying early alterations induced by chemical exposure, which can revolutionize both monitoring and toxicological assessment. The aim of this session is to provide novel insights on the mechanisms of action of immunotoxic compounds focusing on microRNA and microvesicles. Recently, differential expressions of miRNAs and association with several immunologic and inflammatory disorders have been reported, which have important implications in immunotoxicology assessment. miRNAs can influence regulatory mechanisms of inflammation in both inducing and contrasting acute and chronic inflammation. In addition, research on microvesicles also is an emerging and developing field. Studies available to date identified several exposures or lifestyle factors able to modify the trafficking of microvesicles, including air pollutants, cigarette smoke, and oxidative stress. The first speaker will guide the audience into the world of microRNAs from discovery to their role in physiological and pathological conditions, with emphasis on tumors and immunosurveillance, to their use as biomarkers. The second speaker will present data showing influences of environmental exposures on EV-encapsulated RNAs and potential links with several adverse health outcomes, including immunotoxicity. The last two speakers will focus on the role of microRNAs in allergic phenomena, both in humans and in experimental models. Challenges, limitations, and opportunities in this emerging field in environmental health sciences will be discussed.

Introduction. Emanuela Corsini, University of Milan, Milan, Italy.

Non-Coding RNAs—From Bench to Bedside. George Calin, University of Texas, Houston, TX.

Effects of Environmental Exposures on Microvesicles Release and Their Contents. Andrea Baccarelli, Columbia University, New York, NY.

Circulating microRNAs and Prediction of Airway Hyperresponsiveness. Kelan Tantisira, Harvard Medical School, Boston, MA.

microRNA in Experimental Models of Chemical Sensitization. Stacey Anderson, NIOSH, Morgantown, WV.

Toxicological Implication of Copper in Neurodegenerative Diseases

Monday, March 12, 9:15 AM to 12:00 Noon

Chairperson(s): *Masashi Kitazawa, University of California Irvine, Irvine, CA; and Wei Zheng, Purdue University, West Lafayette, IN.*

Primary Endorser:
Metals Specialty Section

Other Endorser(s):
Neurotoxicology Specialty Section

Copper (Cu) is an essential transition metal and required for many normal physiological functions, including energy production, free radical scavenging, connective tissue production, iron mobilization, and neurotransmission. However, excessive intake due to occupational or environmental exposure to divalent Cu(II) has been implicated as a risk for various human diseases. When administered, almost all Cu ions are bound to ceruloplasmin (Cp), and the remainder, non-Cp bound Cu (labile Cu), is bound to albumin, transcuprein, various peptides, and amino acids in plasma. For its chemical reactivity, the plasma level of free Cu is tightly controlled by the above-mentioned Cu-binding proteins. Recent studies have clearly indicated that environmental exposure to Cu in adults accelerates cognitive decline and may increase the risk of developing Alzheimer's disease (AD)-like neuropathology by elevating non-ceruloplasmin-bound Cu in plasma. This session will bring together the experts who are actively engaging in investigating chemistry of Cu in biological systems, Cu neurotoxicity, and its underlying cellular and molecular mechanisms to discuss the toxicological implications of Cu in neurodegenerative diseases. After a brief introduction of Cu in health and human diseases, the first speaker will highlight the mechanisms by which Cu is transported in and out of the brain through the blood-brain barrier (BBB) and blood-CSF barrier and how the altered Cu transport processes in brain barriers may cause Cu dysregulation, leading to Parkinsonian disorders (PD). The second speaker will present new evidence that Cu controls MMP activity and CLUT-1 levels and how these changes lead to BBB dysfunction in the aged brain in conjunction with the role of Cu in regulating the endothelial lipoprotein receptor-related protein 1 (LRP1) as one possible mechanism

increasing the risk for AD. The third speaker will further expand the subject by addressing the immunomodulatory and multifactorial influences of Cu on Aß clearance in the brain and how microRNAs play a critical role in the Cu-mediated down-regulation of LRP1 in the endothelial cells. The fourth speaker will focus on the unique structural chemistry of Cu in its interaction with Aß and how copper positions within the fibrillary structure of Aß and promotes its assembly by using highly sophisticated nanoscience technology. The final speaker will introduce the role of Cu in adult neurogenesis in the subventricular zone. New data unveiling the mechanism by which Cu regulates the critical steps leading to migration and differentiation of neural stem cells in the SVZ-rostral migratory stream pathway, and possible implication in the involvement of Cu in PD, also will be presented. Overall, this session will present the latest findings on the structural, genetic, cellular, and molecular mechanisms of Cu neurotoxicity linking neurodegenerative diseases such as AD and PD. The session will capture the broad interest of those engaged in toxicological research of neurodevelopment and neurodegenerative diseases, neuroscience, neurotoxicology, metal biology, and nanoscience.

Regulation of Copper Homeostasis by the Brain Barrier Systems: Implications in Neurodegenerative Diseases. Andrew Monnott, Cardno-ChemRisk, San Francisco, CA.

Brain Capillary Copper and the Accumulation of CNS Proteins Associated with Neurodegeneration and Dementia. Rashid Deane, University of Rochester, Rochester, NY.

Multifactorial Role of Copper Toxicity on Modulating Amyloid-Beta Clearance Via microRNA and Inflammation. Masashi Kitazawa, University of California Irvine, Irvine, CA.

Amyloid-Copper Complexes and Approaches to Heterogeneity in Biological Systems. Paul Weiss, University of California Los Angeles, Los Angeles, CA.

Does Copper Play a Role in Adult Neurogenesis in Subventricular Zone? Wei Zheng, Purdue University, West Lafayette, IN.

Understanding the Molecular Mechanisms of Zika Virus Reproductive and Developmental Toxicity

Monday, March 12, 9:15 AM to 12:00 Noon

Chairperson(s): *Pedro Del Valle, US FDA, Silver Spring, MD; and Elena Hernandez-Ramon, NIH, Bethesda, MD.*

Primary Endorser:
Reproductive and Developmental Toxicology Specialty Section

Other Endorser(s):
Biotechnology Specialty Section
Clinical and Translational Toxicology Specialty Section

Zika virus (ZIKV) is related to the Yellow fever, West Nile, Japanese encephalitis, and Dengue fever viruses, all classified under the genus Flavivirus that belongs to the family Flaviviridae. Symptoms of infection may include a rash, itching, fever, muscle pain, conjunctivitis, nausea, vomiting, and headaches. ZIKV was isolated from a rhesus macaque in the Zika forest in Uganda in 1947, from mosquitos in 1948 in Africa, from Asian countries in the 1960s, and reached the Americas in 2015. Outbreaks have been reported in Micronesia (2007), French Polynesia (2014), and Brazil (2015). By January 2016, autochthonous cases of ZIKV were reported in more than 50 countries in South, Central, and North America, and the Caribbean, with more than 35,000 cases of the mosquito-borne disease in the United States. ZIKV in pregnant women is reported to cause a wide spectrum of fetal malformations, collectively called congenital Zika syndrome (CZS), that include microcephaly, absent or poorly developed brain structures, retinal damage, hearing deficits, and impaired growth. This session will explore recent findings that have begun to link ZIKV infection with male testicular damage and potential human male infertility and with congenital malformations, microcephaly, and other brain malformations and birth defects. The session also will include an integral discussion of pre-clinical trials and the role of vector control approaches to reduce/prevent ZIKV infection. The introduction will include a brief overview of the ZIKV infection during outbreaks, with emphasis on the current status of the outbreak in the Americas. ZIKV is primarily spread by the daytime-active female *Aedes aegypti* mosquito, and several mechanisms of ZIKV replication and tissue tropism are being investigated. Evidence that ZIKV requires the ubiquitin-proteasome system for replication and the hijacking of the host ubiquitin system will be discussed. Understanding the molecular mechanisms of replication is critical to identifying existing or developing new drugs that can prevent or stop viral infection. ZIKV can spread from mother to child during pregnancy or at delivery. Infection during pregnancy is reported to cause CZS; scientists in Brazil used pregnant SJL mice to provide evidence that the Brazilian ZIKV strain crosses the placenta, infects fetuses, and causes microcephaly by targeting cortical progenitor cells, inducing cell death by apoptosis and autophagy, resulting in impaired neurodevelopment. Research continues to further understand the mechanisms of fetal infection and pathogenesis to identify prevention methods, as the cases of newborns with congenital malformations rise. ZIKV infection also is spread by sexual transmission, especially from symptomatic men to women through the semen. A male mouse model of ZIKV infection was developed by scientists at Washington University in St. Louis to show that ZIKV destroys testicular germ cells, which results in reduction of testosterone levels, inhibin B levels, sperm count, and fertility. The potential impact of the virus on the reproductive health of infected men is unclear, and further research is needed. The US Zika pregnancy registry reported that from 2016 to August 2017, there were 1,784 completed pregnancies with or without birth defects, of which there were 91 liveborn infants and eight pregnancy losses with birth defects, all with laboratory evidence of possible ZIKV infection. The international concern for the fast emergence of ZIKV infection prompted global efforts to find solutions for the ZIKV threat. Approaches include testing current antiviral treatments, developing new drugs, developing vaccines, and implementing vector control strategies. A limited number of drugs and antiviral compounds have been identified using the drug re-purposing screen approach, though drug development has not progressed as fast as expected. Vaccine development for ZIKV has advanced rapidly, capitalizing on previous vaccine development programs for similar diseases like West Nile, Chikungunya, Dengue, and Ebola. Vector control strategies have included a wide-range of mosquito-control methods, such as personal protective measures, breeding environment reduction and larval control, and biological and chemical adulticides measures. Speakers will show that further understanding of the underlying mechanisms of infection and reproductive and developmental toxicity will aid in the design of potential therapies to prevent birth defects; timely implementation of vector control strategies may be effective in the prevention and reduction of ZIKV infection.

Introduction: A Brief Overview of Zika Virus Infection and Current Magnitude of Infection. Pedro Del Valle, US FDA, Silver Spring, MD.

The Role of the Host Ubiquitin System in Zika Virus Replication and Tissue Tropism. Ricardo Rajsbaum, University of Texas Medical Branch, Galveston, TX.

Zika Congenital Syndrome in Murine Experimental Model. Jean Pierre S. Peron, University of São Paulo, São Paulo, Brazil.

Mouse Model of Zika Virus Infection in Testis and Its Potential Relevance to Mechanism of Infection in Human Testis and Male Infertility. Prabagran Esakky, Washington University School of Medicine in St. Louis, St. Louis, MO.

Protective Efficacy of Multiple Vaccine Platforms against Zika Virus Challenge in Rhesus Monkeys. Rafael Larroca, Harvard Medical School, Boston, MA.

Integrated Pest Management: A Multifaceted Approach to Vector Control. Elizabeth Mendez, US EPA, Washington, DC.

Workshop Sessions

Assessing the Dose of Particles in Toxicological Studies: Advances in Dosimetry Models for *In Vitro* and *In Vivo* Applications in Light of Risk Assessment

Monday, March 12, 9:15 AM to 12:00 Noon

Chairperson(s): *Flemming Cassee, Rijksinstituut voor Volksgezondheid en Milieu (RIVM) and University of Utrecht, Bilthoven, Netherlands; and Justin Teeguarden, Pacific Northwest National Laboratory, Richland, WA.*

Primary Endorser:
Inhalation and Respiratory Specialty Section

Other Endorser(s)
***In Vitro* and Alternative Methods Specialty Section**
Risk Assessment Specialty Section

Emerging hybrid, experimental/computational approaches to cellular dosimetry can be used by particle toxicologists to accurately calculate the delivered dose to cells for various particles and under different *in vitro* experimental conditions as a function of exposure time. Likewise, *in vivo* lung dosimetry models allow researchers to estimate the delivered particle dose in any region of the respiratory system, as well as study the implications of particle properties and breathing parameters for diverse animal species. Moreover, knowing the deposited dose also will facilitate the extrapolation from experimental animals (rat, mouse, rabbit, pig, and monkey) to humans of all ages. Most importantly, incorporating such dosimetric methodologies in the study design enables particle toxicologists to bring *in vitro* and *in vivo* doses to the same scale, an important step towards the development and validation of *in vitro* cellular screening assays.

Introduction: Needs for *In Vitro* Modeling for Risk Assessment. Justin Teeguarden, Pacific Northwest Laboratory, Richland, WA.

Advances in *In Vitro* Particle Dosimetry Continuum to Assess the Dose Based on Concentrations. Philip Demokritou, Harvard T.H. Chan School of Public Health, Boston, MA.

Demonstration: A Standardized, Integrated Methodology across the ENM Dispersion Preparation-Colloidal Characterization-Cellular Dosimetry. Glen Deloid, Harvard T.H. Chan School of Public Health, Boston, MA.

Modeling the Dose (Rate) in Rodents and Humans Including Demonstrations. Flemming Cassee, National Institute for Public Health and the Environment (RIVM) of the Netherlands and University of Utrecht, Bilthoven, Netherlands.

Defining the Dose of Particles in Toxicological Studies: Applications of Advances in *In Vitro* and *In Vivo* Dosimetry Models in Risk Assessment. Günter Oberdörster, University of Rochester, Rochester, NY.

Fate of Inhaled Particle-Gas Mixture in the Respiratory Tract. Bahman Asgharian, Applied Research Associates, Raleigh, NC.

Predicting Drug-Induced Cholestatic Injury in Humans

Monday, March 12, 9:15 AM to 12:00 Noon

Chairperson(s): *James McKim, Western Michigan University Homer Stryker M.D. School of Medicine and IONTOX, Kalamazoo, MI; and Mathieu Vinken, Vrije Universiteit Brussel, Brussels, Belgium.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

Other Endorser(s):
Mechanisms Specialty Section

Drug-induced liver injury is a major reason of failure during the premarketing and postmarketing phases of drug development. Being responsible for more than 50% of all cases of acute liver failure worldwide, drug-induced liver injury is equally of high clinical concern. As such, up to 40% of drug-induced liver injury patients present a cholestastic liver insult pattern. Cholestasis is derived from the Greek words chole and stasis meaning bile and halting, respectively, and denotes any situation of impaired bile secretion with concomitant accumulation of noxious bile acids in the liver or systemic circulation. Drug-induced cholestasis typically, though not uniquely, starts by inhibition of one or more drug transporters directly leading to bile acid retention in the liver. This triggers a deteriorative response associated with oxidative stress, inflammation, and cell death. In parallel, an adaptive response is initiated, which is aimed at restricting bile acid synthesis and influx, while promoting bile acid efflux. In fact, these mechanisms have been embedded recently in an adverse outcome pathway construct in order to further facilitate predictive toxicology. Several additional key events in drug-induced cholestatic liver injury have been identified, including endoplasmic reticulum stress and mitochondrial impairment. Simultaneously, a number of human-based *in silico* (e.g., DILIsym), *ex vivo* (e.g., precision-cut liver slices), and *in vitro* (e.g., sandwich cultures of human hepatocytes and two-compartment systems) models have been introduced to mechanistically study drug-induced cholestatic injury. Such alternative animal-free models are cordially welcomed, not only because of ethical reasons, but also given the fact that preclinical animal models are not adequate predictors of human drug-induced liver injuries due to interspecies differences in bile acid profiles, transport, and regulation. These non-animal methods, especially when combined, are able to accurately and quantitatively predict drug-induced cholestatic liver injury, thus emphasizing their overall clinical relevance.

'Omics-Based *In Vitro* Verification of an Adverse Outcome Pathway of Cholestatic Liver Injury. Mathieu Vinken, Vrije Universiteit Brussel, Brussels, Belgium.

Mechanistic Modeling of Cholestasis: Clinical Relevance. Kim Brouwer, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Precision-Cut Liver Slices as Model for Drug-Induced Cholestasis. Geny Groothuis, University of Groningen, Groningen, Netherlands.

Prediction of Cholestatic Hepatotoxicity: Integration of Transporter Regulation and Adaptive Response. Kenneth Brouwer, Qualyst Transporter Solutions, LLC, Durham, NC.

An Integrated *In Vitro* Organ Platform to Evaluate Cholestasis. James McKim, Western Michigan University Homer Stryker M.D. School of Medicine and IONTOX, Kalamazoo, MI.

Toxicology's Next Grand Challenge: Embracing Exposure Science for Effective Public Health Protection

Monday, March 12, 9:15 AM to 12:00 Noon

Chairperson(s): *Claire Terry, Dow AgroSciences, Indianapolis, IN; and Timothy Gant, Public Health England, Chilton, United Kingdom.*

Primary Endorser:
Risk Assessment Specialty Section

Other Endorser(s):
Occupational and Public Health Specialty Section
Regulatory and Safety Evaluation Specialty Section

The human health risk assessment paradigm is changing, and one important aspect of this is the focus upon the exposure element of risk assessments. To date, the greater weight has generally been on hazard in the risk assessment process, with exposure being considered retrospectively. The result is the expenditure of considerable time, effort, and resources on acquiring hazard information that ultimately is not always required to reach conclusions on the safety of a chemical. Scientists have been working to develop exposure and risk assessment methods and tools to change this paradigm; however, a limiting factor is that exposure assessments are specific to the chemical use pattern/scenario, and this can lead to "silos" in approaches and knowledge. This session aims to bring together different sectors (agrochemicals, consumer products, industrial chemicals) and regulators who need exposure data and leverage approaches across these sectors. The scene will be set by the first two presenters, who will describe their vision for integrating advanced exposure science into public health assessment. The next three presentations will focus on approaches and techniques, with case studies, used in the exposure science of chemicals. Current and innovative methods (for example, *in silico* methods, toxicokinetics, PBPK, IVIVE, biomonitoring data) and their potential application to regulatory frameworks will be discussed. This session aims to provide a forum for academic researchers, industry scientists, and regulators to present and discuss recent advances in the area of exposure assessment for chemicals. The session will conclude with charge questions for discussion by the panel and audience members and will identify key areas/topics/gaps that should be considered further.

Introduction. Claire Terry, Dow AgroSciences, Indianapolis, IN.

Advancing Exposure's Profile in Providing the Context for Toxicity Testing and Risk Assessment. Jennifer Orme-Zavaleta, US EPA, Research Triangle Park, NC.

The Goals of Exposome Research and Examples from Europe. Paulo Vineis, Imperial College London, London, United Kingdom.

The Importance of Exposure Considerations in Safety Assessment. Andrew Scott, Unilever, Surrey, United Kingdom.

Application of the Aggregate Exposure Pathway and Adverse Outcome Pathway Frameworks to Advance Cumulative Risk Assessment by Integrating Human Health and Ecological Endpoints. David Hines, US EPA, Washington, DC.

How Exposure-Based Refinements Can Benefit the 3Rs. Fiona Sewell, NC3Rs, London, United Kingdom.

Informational Sessions

Changes to the Common Rule Regulations and Implications for Human Research

Monday, March 12, 12:10 PM to 1:30 PM

Chairperson(s): *Michael Madden, US EPA, Chapel Hill, NC; and Daniele Wikoff, ToxStrategies, Asheville, NC.*

Primary Endorser:
Clinical and Translational Toxicology Specialty Section

Other Endorser(s):
Ethical, Legal, Forensics, and Societal Issues Specialty Section

The regulations that govern research involving human subjects are known as the "Common Rule" because they are shared in common by 18 federal departments and agencies that conduct and support such research [The US Food and Drug Administration is not a signatory to the Common Rule]. These regulations have not changed substantively since 1981. During that time, the research they cover has evolved considerably, with new scientific techniques and new ethical challenges that do not always fit well under the established structure. These include an evolving concept of what constitutes identifiable information and biospecimens, techniques such as whole genome sequencing, and concerns over commercialization and informed consent. A six-year rulemaking process began in 2011, with a preliminary draft notice release and more than 3,000 public comments received. This process culminated in the publication of a revised final rule on January 19, 2017. The majority of changes will take effect in January 2018, bringing sweeping changes for scientists and their institutions, funding agencies, and the Institutional Review Boards (IRBs) that oversee this work. This informational session will review the reasons for change, the rulemaking process, and the major changes in the revised regulations with a presentation by the US Environmental Protection Agency representative on the Interagency Working Group that crafted the new Common Rule. The daily experiences of implementing the Common Rule changes in a timely manner into human subject research at an academic institution and areas where the new rule is not clear will be shared by a presenter with the Office of Clinical Research at the University of Texas Health Science Center at San Antonio (UT Health San Antonio). UT Health San Antonio has several IRB authorization agreements with nearby institutions, such as Brooke Army Medical Center and the Southwest Research Institute, to serve as the single IRB of record for collaborative research. Potential issues with implementation of the new rule with studies at collaborative sites will be presented. A third speaker from the National Institute of Environmental Health Sciences IRB will discuss the potential impact of the new Common Rule on the submission and implementation of grant applications and also will provide insights on possible upcoming changes in the National Institutes of Health processes for human studies. This session will present extremely important ethics information for those who perform research with human subjects, including industry, government, and academia, and will facilitate discussions about applicability of the changes to current research and potential research designs and submissions. *Disclaimer: The views expressed are those of the authors and do not necessarily represent the views or policies of the US EPA.*

Introduction. Michael Madden, US EPA, Chapel Hill, NC.

Revising the Common Rule: What Is It, How Did We Get Here, and Where Are We Going? Daniel Nelson, US EPA, Chapel Hill, NC.

Implementing the Changes in the Common Rule at an Academic Medical Center. Kimberly Summers, University of Texas Health Science Center at San Antonio, San Antonio, TX.

NIH Human Subject Research: Changes, Challenges, and Expectations. Kimberly Gray, NIEHS, Durham, NC.

Management of Toxic Wastes in Africa: Challenges and Opportunities

Monday, March 12, 12:10 PM to 1:30 PM

Chairperson(s): *Abdel-Razak Kadry, US EPA, Washington, DC; and Bernard Gadagbui, University of Cincinnati, Cincinnati, OH.*

Primary Endorser:
Toxicologists of African Origin Special Interest Group

Africa is the world's second largest and second most populous continent, with a population of 1.2 billion people. In spite of its vast natural resources, Africa faces endemic poverty, food insecurity, and pervasive underdevelopment, with almost all countries lacking the human, economic, and institutional capacities to effectively and sustainably develop and manage their resources. In Africa, use of chemicals has taken a central stage in improving health, agriculture, mining, education, research, and many industrial processes. While African countries are heavy users of industrial chemicals, there is an absence of effective chemical waste management systems, as well as chemical safety education and rigorous enforcement of safety regulations. This absence has the potential to contribute to the exposure of a large portion of the population to toxic chemicals. Users and non-users of chemicals risk exposure to toxic chemicals as a result of ignorance of the risks, failure to employ protective measures, and ineffective implementation and enforcement of safety regulations of these chemicals. It was, thus, not surprising when the World Health Organization published alarming findings in 2014 of the results of a survey of 40 African countries on chemicals of public health risk concern and their management. Many chemicals of public health concern that are banned, controlled, or withdrawn in the developed countries are still in use or shipped for disposal to Africa. These hazardous and toxic wastes pose risks to nearby water, soil, and air and have the potential to cause serious environmental and human health impacts. In addition, there are thousands of tons of industrial waste, containing hazardous chemicals, that are improperly discharged or emitted into the environment. In many African countries, industrial waste in liquid form is usually discharged into sewer systems or rivers as effluent, while solid waste is either dumped in landfills or pits within workplace premises or close to residential areas. In addition, international illegal dumping remains a prevalent issue in chemicals management in Africa. Many African countries lack appropriate, cost-effective, and economically viable technology for chemical waste recycling and disposal. The survey reported the absence of sanitary landfills in some African countries. The future of waste management in Africa is brighter than the present state. While many developing countries have no dedicated hazardous landfill disposal facilities, a few countries (for example, South Africa, Egypt, and Ethiopia) have hazardous landfill disposal facilities. The effectiveness of disposal practices in some cities in these countries could be transferred to other African countries. In light of the circumstances described above, this session will bring attention to the status of hazardous and toxic waste management in Africa and the potential to harness resources for effective management of such wastes on the continent. This will be accomplished

by presentations by a number of African experts in the area of toxicology and toxic waste disposal. The following topics will be discussed within the context of the problem: 1) scope and status of hazardous and toxic waste problems in Africa; 2) challenges, including geographical, that keep Africa behind the developed world in toxic waste disposal and management; 3) the public health implications from the failure of proper toxic waste disposal in Africa; 4) case studies of successful toxic waste disposal in some African countries and methods to transfer the success to other developing countries; and 5) lessons learned, mitigation strategies, strategic planning, networking, and partnering opportunities. The outcome of the session will be a report detailing strategic planning strategies and recommendations from the presenters and participants in the session. The leaders of Toxicologists of African Origin Special Interest Group and its sister organization the African Society for Toxicological Sciences will play a role in planning, facilitating, and disseminating the recommendations to scientists in Africa and the African governments.

The Adverse Health Effects Associated with Living in the Vicinity of Toxic Waste Dump Sites in Africa. Salah Soliman, Alexandria University, Alexandria, Egypt.

Management of Toxic Waste in Ghana: Challenges and Opportunities. Edith Clarke, FZ Safety and Health Centre, Accra, Ghana.

Toxic Waste Management in Cameroon. Asongalem Acha, University of Buea, Buea, Cameroon.

Solid Waste Management in Sub-Saharan Africa: Our Experience in the Kingdom of Swaziland. Sameer Sakallah, Global Biotechnology Solutions, Chantilly, VA.

Mining Industry and Water Contamination in South Africa: Recommended Remediation Approaches. Mary Gulumian, National Institute for Occupational Health, Johannesburg, South Africa.

Panel Discussion/Q&A. Darryl Hood, Ohio State University, Columbus, OH.

Moving Beyond Theory to the Use of Systematic Review to Support Regulatory Decision Making for Evidence-Based Risk Assessment

Monday, March 12, 12:10 PM to 1:30 PM

Chairperson(s): *Daniele Wikoff, ToxStrategies, Asheville, NC; and Katya Tsaioum, Johns Hopkins Bloomberg School of Public Health Evidence-Based Toxicology Collaboration, Watertown, MA.*

Primary Endorser:
Food Safety Specialty Section

Other Endorser(s):
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

The use of systematic review and evidence-based methodologies in toxicology and risk assessment have evolved from theory to practice. This informational session seeks to provide an overview of the landscape of the use of systematic review in regulatory decision making. Recognizing that there are many efforts to advance the science in this arena, this session will focus on efforts specifically associated with risk-based practices, such as development of health-based benchmarks (e.g., acceptable daily intakes, reference doses, etc.) rather than characterization of potential hazard (e.g., likelihood to be a hazard to humans for a given health outcome). Tools and frameworks initially developed for the field of medicine have been adapted for application to toxicological research questions, and in many cases, new tools have been developed. The presentations will describe how the regulatory practitioners have addressed the challenges of toxicological data relative to that of medicine. Examples will include addressing challenges in evaluating exposures vs. interventions, multi-endpoint vs. single-endpoint outcomes, well-defined diseases or conditions, complex data that is often not in humans (but rather in experimental animal studies or *in vitro* studies) vs. randomized controlled trials in humans, and evaluation of mixtures vs. pure substances. Beyond evaluation of individual studies and qualitative characterizations of hazards, approaches to integrate data in the context of risk—to be evaluated on a common metric, to develop health based-benchmarks—have been developed and applied. These concepts must be balanced with the rigor of a systematic review, a component which translates into time and resources. It is anticipated that this session will provide practical information for toxicologists and risk assessors and facilitate an understanding of how systematic review is being utilized in support of risk-based chemical assessments. Notably, speakers also will highlight how systematic review provides additional rigor and transparency, as well as relevance, of the process in decision making for regulated chemicals.

An Introduction to the Integration of Systematic Review to Support Development of Health-Based Toxicity Values in Chemical Risk Assessments. Daniele Wikoff, ToxStrategies, Asheville, NC.

Systematic Review in Support of Chemical Risk Assessment at the EFSA. Elisa Aiassa, European Food Safety Authority (EFSA), Parma, Italy.

Operationalizing Pragmatic Systematic Review in Support of Chemical Risk Assessment at the US EPA. Kristina Thayer, US EPA, Washington, DC.

Guidelines for Performing Systematic Reviews in the Development of Toxicity Factors. Heather Reddick, Texas Commission on Environmental Quality, Austin, TX.

Summary of Global Efforts and Remaining Opportunities to Advance the Field. Katya Tsaioun, Johns Hopkins Bloomberg School of Public Health Evidence-Based Toxicology Collaboration, Watertown, MA.

Symposium Sessions

Adipocyte Toxicology and Obesogens

Monday, March 12, 1:45 PM to 4:30 PM

Chairperson(s): *Supriya Kulkarni, Yale University, New Haven, CT; and Laura Armstrong, Rutgers, The State University of New Jersey, Piscataway, NJ.*

Primary Endorser:
Stem Cells Specialty Section

Other Endorser(s):
***In Vitro* and Alternative Methods Specialty Section**
Mechanisms Specialty Section

The obesity epidemic and associated co-morbidities are becoming an increasing concern to public health. Obesity can be generally defined by excess storage of lipids in adipose tissue. Central adipose tissue content directly correlates with the development of metabolic syndrome and cardiovascular complications that alter adipose tissue metabolism. Adipose tissue is not only a storage depot for triglycerides, but is a metabolically active organ that is responsible for the release of energy to tissues, such as liver and skeletal muscle, by hormonal-signaling pathways. In addition to lipid metabolism and mobilization, adipose tissue is intricately involved in glucose homeostasis and, therefore, contributes overall to the maintenance of systemic energy balance. It is suggested that adipose tissue plays an important role in the development of obesity-related diseases, thus requiring greater knowledge and understanding of adipose tissue development, signaling pathways, and identification of roles in systemic diseases. Current toxicological findings implicate a role for multiple persistent environmental chemicals, such as phthalates, tributyltin (TBT), and Di-(2-ethylhexyl) phthalate (DEHP) in promoting adiposity. Increases in adiposity are attributed to dysregulation of various metabolic pathways via genetic/epigenetic alterations, as well as contributing environmental factors. Recent studies have demonstrated accumulation of persistent environment toxicants due to their lipophilicity in adipose tissue, making adipocytes and preadipocytes targets of toxicity. Many of these studies have established the diverse mechanisms by which "obesogens" promote adiposity. Overall, toxicants appear to have direct and indirect effects on adipose tissue homeostasis and adipose tissue dysfunction, a key characteristic of obesity and hallmark of metabolic disease. Many compounds have been identified via high-throughput screening programs focusing on target-specific binding. These programs include ToxCast, Tox21, and, more recently, the Endocrine Disruption Screening Program. Prioritizing these chemicals for further *in vivo* research is essential due to the number of identified chemicals by these programs. Discerning the cellular and molecular endpoints and physiological outcomes of these chemicals is paramount in toxicological research. The objective of this symposium is to present an overview of the effect of obesogens or endocrine-disrupting chemicals on adiposity. Future research is warranted to contribute to understanding the crosstalk between adipose and other metabolically important tissues (liver, skeletal muscle, intestine) and the overall contribution to a growing obesity epidemic in both adults and children worldwide. *In utero* exposure outcomes to TBT pertaining to the development of a "thrifty genotype" and phthalate exposure effects on adipocyte differentiation and maturation will be discussed, demonstrating the importance of adipocyte development. The major adipocyte regulator PPARγ can be induced by environmental ligands favoring white adipocyte development, while dichlorodiphenyltrichloroethane exerts its effects on brown adipose tissue and the inhibition of thermogenesis, demonstrating the diversity of adipose tissue function. Adipose tissue is responsive to endocrine disruptors; therefore, it is important to also understand the sex-dependent differences in human adipose function and distribution. Lastly, the implications of adipocyte research in regards to regulatory standards and the testing of compounds for adipogeneic properties must be optimized and standardized utilizing specific assays that can correlate to and/or identify obesogens. Medium-throughput assays with greater relevance to downstream cellular outcomes in context to PPARγ and glucocorticoid signaling could be the future of prioritizing adipogeneic compounds for risk assessment. The speakers will introduce the overall importance of adipose tissue homeostasis for human health and the contribution of environmental toxicants to its dysregulation.

Introduction. Supriya Kulkarni, Yale University, New Haven, CT.

Prenatal Obesogen Exposure Leads to a Transgenerational Thrifty Phenotype in Mice. Bruce Blumberg, University of California Irvine, Irvine, CA.

Plasticizer-Induced Changes in Adipocyte Differentiation and Function. Vassilios Papadopoulos. University of Southern California, Los Angeles, CA.

Environmental PPARγ Ligands: Inducers of White, but Not Brite, Adipogenesis. Jennifer Schlezinger, Boston University School of Public Health, Boston, MA.

Sex and Depot Differences in Adipocyte Biology. Susan Fried, Icahn School of Medicine at Mount Sinai, New York, NY.

Evidence That the Pesticide DDT and Its Metabolite DDE Are Obesogens. Michele La Merrill, University of California Davis, Davis, CA.

Screening ToxCast and Tox21-Prioritized Chemicals for Mechanistic Function in a Human Adipose-Derived Stem Cell Model of Adipogenesis. Chad Deisenroth, US EPA, Durham, NC.

Alternative Testing Strategies for Nanomaterials and Ultrafine Particles

Monday, March 12, 1:45 PM to 4:30 PM

Chairperson(s): *Monita Sharma, PETA International Science Consortium Ltd., London, United Kingdom; and Justin Teeguarden, Pacific Northwest National Laboratory, Richland, WA.*

Primary Endorser:
Inhalation and Respiratory Specialty Section

Other Endorser(s):
***In Vitro* and Alternative Methods Specialty Section**
Risk Assessment Specialty Section

Inhalation represents the primary route of exposure to aerosolized nanomaterials (NMs) and ultrafine particles in humans. The increasing use of NMs in consumer-based products warrants a thorough evaluation of their biological impacts and a need to test a large number of different types of NMs. Due to the substantive time, cost, and animals required to conduct traditional *in vivo* toxicity tests, there is much interest in developing human-relevant strategies that are less reliant on the use of animals to assess the toxicity of these materials for various risk assessment applications. This session will include presentations on *in vitro* systems that are

currently being used to assess the inhalation toxicity of nanomaterials and ultrafine particles. Additionally, presenters will discuss the parameters that are critical to consider while designing *in vitro* systems and which facilitate their interpretation and application in risk assessment, including the following: dosimetry, aerosol generation and exposure, appropriate cell types, and identification of relevant endpoints. Contribution of adverse outcome pathways (AOPs) to experimental and regulatory toxicology of NMs and strategies for the development of AOPs, as well as associated issues and limitations, also will be discussed. By discussing the aforementioned parameters, this session will provide an insight into the factors that should be considered to increase the ability of *in vitro* methods to predict human outcomes, eventually leading to their use in regulatory decision making.

Introduction. Monita Sharma, PETA International Science Consortium Ltd., London, United Kingdom.

Integrated *In Vitro-In Vivo* Models for Nanomaterial and Ultrafine Particle Toxicity Testing: Moving from a Screening Hazard Tool to Predictive Models for *In Vivo* Adverse Effects. Todd Stueckle, NIOSH, Morgantown, WV.

Predictive 3D Lung Models to Assess the Toxicity of Inhaled Nanoparticles. Barbara Rothen-Rutishauser, University of Fribourg, Fribourg, Switzerland.

Contemporary Considerations in Engineered Nanomaterial Characterization, Aerosol Generation, and Exposure. Christie Sayes, Baylor University, Waco, TX.

An Integrated Methodology across the Dispersion Preparation-Colloidal Characterization-Cellular Dosimetry Continuum for Engineered Nanomaterials. Philip Demokritou, Harvard T.H. Chan School of Public Health, Boston, MA.

Dosimetry Modeling to Aid *In Vitro* to *In Vivo* Extrapolation (IVIVE) of Inhaled Nanomaterials for Risk Assessment Applications. Annie Jarabek, US EPA, Research Triangle Park, NC.

Advances in Developing Adverse Outcome Pathways to Assess Inhalation Toxicity of Nanomaterials. Sybille Brule, Louvain Centre for Toxicology and Applied Pharmacology, Brussels, Belgium.

Highlights and Conclusions from the Session. Justin Teeguarden, Pacific Northwest National Laboratory, Richland, WA.

Chemical Grouping for 21st-Century Toxicology, Risk Assessment, and Decision Making

Monday, March 12, 1:45 PM to 4:30 PM

Chairperson(s): *Jane Ellen Simmons, US EPA, Research Triangle Park, NC; and Mark Nelms, Oak Ridge Institute for Science and Education, Oak Ridge, TN.*

Primary Endorser:
Mixtures Specialty Section

Other Endorser(s):
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

"Grouping" is a generic term describing placing chemicals in groups based on characteristics or factors that the assembled chemicals have in common to enable consideration of more than one chemical at the same time. Developing chemical groups is necessary for a variety of useful purposes, including something as seemingly simple, but as critically important, as safe chemical storage. Key uses of grouping in toxicology, risk assessment, and decision making include identification of co-occurring chemicals in the environment, the body, or the exposome; creating and prioritizing groups for chemical mixtures toxicology and mixtures risk assessment; and identifying chemicals that are toxicologically similar (i.e., that share the same adverse outcome pathway (AOP) or have AOPs that start with different molecular initiating events (MIEs), but converge later in the pathway) or are toxicologically independent. Another important use is developing groups that facilitate the filling of data gaps by techniques such as read-across, trend analysis, extrapolation, interpolation, and QSAR; this use of grouping results in reduced experiment effort, saving time, resources, and experimental animals. Grouping also benefits green chemistry and enables the use of molecular design for reducing unwanted toxicity. Traditionally, groups have been based on exposure alone or toxicity alone. Strategies laid out in *Toxicology Testing in the 21st Century: A Vision and a Strategy* (National Research Council [NRC] 2007) and *Exposure Science in the 21st Century: A Vision and a Strategy* (NRC, 2012) and corresponding advances in exposure science, high-throughput toxicology, 'omics sciences, and computational technologies have resulted in a wide array of next generation methods and tools. The purpose of this session is to highlight how these advances are being translated and used in next-generation grouping approaches. In this session, experts from industry, academia, and government will present state-of-the-art insights into new methods currently being developed and employed that have current or future application to chemical groups. The importance of accurate grouping in decision making will be illustrated in the brief introduction. The first full presentation will showcase a novel, fully-integrated text mining-based tool capable of automatically analyzing relevant literature and classifying a given chemical according to its carcinogenic mode of action based on a structured taxonomy. The second talk will focus on using a mechanistic understanding of the interaction between a chemical and the MIE within an AOP, coupled with 2D chemical structure information, to group chemicals and how inclusion of chemical bioactivity profiles may then be used to refine the initial groupings. The third presentation will present the application of the concept of connectivity mapping in a predictive toxicology paradigm, where gene-expression profiles and pattern-matching software are used to find connections between chemicals, adverse events, and genes to group chemicals with similar mechanisms of action. The fourth talk will illustrate how chemical categories associated with specific MIEs can be utilized to guide higher level QSAR methods, such as comparative molecular field analysis, that enable quantitative predictions to be made regarding chemical binding affinity and/or downstream bioactivity without needing to fully elucidate the shape of the binding pocket of the biological target. The final presentation of the session will explore the influence of grouping decisions and misclassification errors that might occur on risk prediction when using the relative potency factors method to assess mixtures risk, focusing on variability introduced if the same (or different) dose-response curve shape is assumed for all chemicals in the group when the shapes truly differ (or are the same) or when independence is assumed for convergent AOPs and the resulting uncertainty of the estimated mixture response. *Disclaimer: The views expressed are those of the authors and do not necessarily represent the views or policies of the US EPA.*

Why Do We Need 21st-Century Grouping Methods? Jane Ellen Simmons, US EPA, Research Triangle Park, NC.

CRAB 2.0: A Text Mining-Based Approach for Grouping Chemicals According to Carcinogenic Modes of Action. Imran Ali, Karolinska Institutet, Stockholm, Sweden.

Adverse Outcome Pathway Networks: Use of 2D Chemical Structure and Bioactivity Profile to Generate Chemical Categories. Mark Nelms, Oak Ridge Institute for Science and Education, Oak Ridge, TN.

Use of Connectivity Mapping (CMap) as a Tool to Group Chemicals Based on Mode of Action. K. Nadira De Abrew, Proctor and Gamble Company, Cincinnati, OH.

Using Chemical Categories to Inform Quantitative Risk Assessment. Timothy Allen, University of Cambridge, Cambridge, United Kingdom.

Estimating the Impact of Grouping Misclassification on Risk Prediction When Using the Relative Potency Factors Method to Assess Mixtures Risk. Jeffery Swartout, US EPA, Cincinnati, OH.

Decoding Oxidative Stress from Inflammation: Implications for Exposure, Toxicity, and Disease

Monday, March 12, 1:45 PM to 4:30 PM

Chairperson(s): *Maria Kadiiska, NIEHS, Research Triangle Park, NC; and Thomas van't Erve, NIEHS, Research Triangle Park, NC.*

Primary Endorser:
Mechanisms Specialty Section

Other Endorser(s):
Neurotoxicology Specialty Section
Reproductive and Developmental Toxicology Specialty Section

Free radical damage, inflammation, and/or oxidative stress have been implicated in numerous toxicity and disease mechanisms. Most of the time, inflammation and oxidative stress are perceived as one and the same. However, current research is proving this perception to be inaccurate and oversimplified. Despite sharing many similarities, the two mechanisms have complex and unique upstream and downstream targets. Failing to distinguish between the two mechanisms is detrimental to accurate data interpretation in experimental animal models of toxicity and human conditions. The translation of this important distinction into *in vivo* and human research has been limited, as has the translation into quantitative aspects of the role of oxidative stress in human disease. However, decoding oxidative stress from inflammation and identifying each mechanism's unique targets are of great consequence because they may ultimately lead to the design and implementation of corresponding appropriate treatment strategies. This symposium will: 1) discuss the mechanistic distribution between oxidative stress and inflammation *in vivo* and in human conditions; 2) define the correct and incorrect interpretation of oxidative stress and inflammation; and 3) outline the progress obtained so far and future directions for this emerging complex field. The chair will present a brief overview on biomarker research and why distinguishing between oxidative stress and inflammation is required for correct biomarker interpretation. The first speaker will discuss redox-signaling implying a fundamental role for NF-κB p50 in the regulation of chronic neuroinflammation by free radicals. Understanding this complex regulatory node is vital in determining how microglia can become a chronic source of inflammation and reactive oxygen species. The contribution of either pathway is vital in understanding progressive neuron and central nervous system damage. The second speaker will show a new approach to quantify the contribution of oxidative stress and inflammation using the lipid peroxidation marker F2-isoprostane in conjunction with prostaglandins. In addition, he will discuss the misinterpretation of mechanism in past literature. Using a meta-analysis, he will present the potential discrepancy between oxidative stress and inflammation in reproductive health, central nervous system diseases, and others. The third speaker will present new findings on the importance of the distinction between inflammation and oxidative stress in an epidemiologic study on birth outcomes. This work is the first large-scale application of the new F2-isoprostane/prostaglandin ratio approach. Correct distinction between the two mechanisms is crucial to accurately identifying future interventions, minimizing the risk for pregnancy complications and compromised infant health. From a more translational perspective, the fourth speaker will discuss the relation between used markers of inflammation and oxidative stress to redox-related diseases. He will show the reasons why antioxidants acting by scavenging ROS might not prevent their detrimental effects and also may interfere with essential signaling roles in clusters of human diseases. Since inflammation, free radical damage, and oxidative stress are not "diseases," distinguishing among them *in vivo* and in human disorders could lead to better interceptive strategies and correct interpretation of the results in former and future studies. While inflammation and oxidative stress are discussed separately in many publications, lectures, and past SOT presentations, the complex cross-talk and importance to distinguish between the two mechanisms is rarely investigated. This session will offer specific approaches to measure, calculate, distinguish, and correctly identify the differences between the effects of oxidative stress and inflammation. The session will propose a classification of exposures, toxicities, and diseases decoded by distinguishing oxidative stress from inflammation.

Biomarkers of Oxidative Stress. Maria Kadiiska, NIEHS, Research Triangle Park, NC.

Role for NF-κB p50 in the Regulation of Chronic Neuroinflammation by Free Radicals. Michelle Block, Indiana University School of Medicine, Indianapolis, IN.

Overcoming Bias in F2-Isoprostane Oxidative Stress Measurement: Quantifying the Contribution of Inflammation. Thomas van't Erve, NIEHS, Research Triangle Park, NC.

Inflammation Differentiated from Oxidative Stress in Reproductive Epidemiology: Understanding the Environmental Impact on Birth Outcomes. Kelly Ferguson, NIEHS, Research Triangle Park, NC.

Emerging Indications of Biomarkers for Use in Humans within a Cluster of Redox-Related Diseases: Relevance of Biomarkers of Oxidative Stress, Inflammation, Antioxidants, and Redox Signaling. Harald Schmidt, Maastricht University, Maastricht, Netherlands.

Estrogen Receptor Signaling as a Mechanism of Developmental Toxicity

Monday, March 12, 1:45 PM to 4:30 PM

Chairperson(s): *Daniel Gorelick, University of Alabama at Birmingham, Birmingham, AL; and Tamara Tal, US EPA, Research Triangle Park, NC.*

Primary Endorser:
Reproductive and Developmental Toxicology Specialty Section

Other Endorser(s):
Molecular and Systems Biology Specialty Section

Estrogens are steroid hormones that influence the development and function of nearly every major organ system in the body—from the gonads to the central nervous system. Xenobiotic agents that mimic estrogens or influence estrogen production or metabolism can exert profound effects on organismal development. Aberrant estrogen receptor signaling is classically associated with reproductive toxicity. However, in the last decade, it has become apparent that abnormal estrogen receptor signaling during development can cause widespread changes in cardiovascular, immune, and metabolic functions. With the development of new molecular tools, improved understanding of developmental biology, and the use of new model organisms, tremendous advances have been made in understanding how estrogen receptors regulate development at the molecular, cellular, and physiological levels. This session will explore cutting-edge research in developmental toxicology, revealing the mechanisms by which estrogen receptors influence organismal development. Using an adverse outcome pathway framework, the speakers will explore estrogen receptor-mediated toxicity from the molecular initiating event (receptor activation) through adverse outcomes, such as organ malformation and dysfunction, thus linking early signaling events to organismal toxicity. The first speaker will discuss new *in vitro* and *in silico* screening approaches to predict and model estrogen receptor toxicity and how these approaches are being used for hazard assessment and testing prioritization and are leading compound development under the new Toxic Substances Control Act guidelines. To evaluate high-throughput estrogen receptor toxicity predictions, novel *in vivo* models are required. The second speaker will present on a novel zebrafish model being used to explore why some embryonic tissues are more sensitive to estrogen exposure than others. The third presentation will outline the similarities and differences by which estrogens and related sex hormones influence gonad development at the molecular and cellular levels and how these mechanisms can be hijacked by exposure to xenoestrogens during critical periods of development. The final two speakers will focus on adverse outcomes and discuss how estrogen receptors influence developmental toxicity in a sexually dimorphic manner with a focus on energy homeostasis and social, sexual, or anxiety-like behaviors in offspring of exposed mothers. These five speakers, using diverse approaches and model systems, will demonstrate how understanding the detailed mechanisms by which estrogen receptors influence developmental toxicology will improve the ability to identify potentially deleterious xenoestrogens and pharmaceutical estrogens with less side effects on patients and their offspring.

Introduction. Daniel Gorelick, University of Alabama at Birmingham, Birmingham, AL.

Large-Scale Screening of Chemicals for Estrogen Receptor Activity: What Have We Learned? Richard Judson, US EPA, Research Triangle Park, NC.

Using Zebrafish *In Vivo* and *In Vitro* Models to Evaluate Estrogenic Endocrine Disruptors. Maria Bondesson, Indiana University, Bloomington, IN.

Estrogen Actions in Zebrafish Gonads: A Delicate Balance. Camerron Crowder, University of Alabama at Birmingham, Birmingham, AL.

Maternal Exposures to Estrogenic Endocrine-Disrupting Compounds Cause Sex-Dependent Effects on Energy Homeostasis. Troy Roepke, Rutgers, The State University of New Jersey, New Brunswick, NJ.

Sexually Dimorphic Effects of Estrogenic Environmental Endocrine Disruptors on the Developing Brain. Andrea Gore, University of Texas, Austin, TX.

High-Throughput Transcript Profiling and Functional Assessment: From Screening to Systems Biology Strategies for Personal Chemical Safety Predictions

Monday, March 12, 1:45 PM to 4:30 PM

Chairperson(s): *Chris Corton, US EPA, Durham, NC; and Bob van de Water, Universiteit Leiden, Leiden, Netherlands.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

Other Endorser(s):
Molecular and Systems Biology Specialty Section

High-throughput screening (HTS) assays are an important component of chemical safety evaluation programs carried out by a number of organizations. However, it is recognized that the assays do not sufficiently cover all potentially important pathways. In the last few years, adaptation of gene expression profiling to high-throughput formats has been increasingly considered an attractive alternative to individual assays due to lower costs and the ability to essentially measure all pathways simultaneously. While microarrays have been used extensively in more focused lower-throughput studies and comprise the bulk of large publicly-available databases, technologies that can measure the targeted expression of the entire genome are emerging as attractive alternatives. Novel computational approaches are increasingly being used to move the field from using transcript profiles as hypothesis-generation tools to accurately predicting effects. Functional genomics strategies that identify gene-chemical interactions in gene-knockdown screens have proven valuable to validate predictions from transcript profiling and to determine species-specific effects. These integrated high-throughput genomics approaches will allow identification of relevant key events that are quantifiable in high-throughput (HT) transcriptomic settings and predict cell and biological changes, as well as human-translational, implications. This session highlights major advances in the field of using transcript profiling and functional genomics in a number of areas important in risk assessment. The first presentation will highlight recent results of a large-scale HT screen of 1,000 chemicals in a human cell line, allowing dose-response modeling of biological pathways on a massive scale. The second and third presentations will describe novel computational approaches which utilize both private and publically available databases to make predictions of molecular targets of chemicals and perturbations in gene networks that lead to toxicity. The last two talks will discuss exciting work which identifies genetic modifiers of responses to

chemicals, allowing assessment of individual susceptibility to chemical injury. This session will be of wide interest, including to scientists interested in the application of gene expression profiling and *in vitro* assays to regulatory decision making.

Introduction. Chris Corton, US EPA, Durham, NC.

High-Throughput Transcriptomics: From Screening to Pathways. Imran Shah, US EPA, Durham, NC.

Identification of Potential Chemical Carcinogens in Compendia of Gene Expression Profiles. Chris Corton, US EPA, Durham, NC.

Reducing Noise and Boosting Biological Signal Detection in Large Transcriptomic Datasets. James Stevens, Lilly Research Laboratories, Indianapolis, IN.

High-Throughput Identification of Genotype-Specific Vulnerabilities to Drug Treatment. Chris Mader, Broad Institute of MIT and Harvard, Cambridge, MA.

Functional Genomics of Cellular Stress Pathways: Towards a Personalized Chemical Safety Assessment. Bob van de Water, Universiteit Leiden, Leiden, Netherlands.

Revising Biology: Using Genomic and Epigenomic Editing to Gain Novel Insight into the Molecular Mechanisms of Toxic Exposure Effects and Susceptibility

Monday, March 12, 1:45 PM to 4:30 PM

Chairperson(s): *Shaun McCullough, US EPA, Chapel Hill, NC; and Marie Fortin, Rutgers, The State University of New Jersey, Piscataway, NJ.*

Primary Endorser:
Molecular and Systems Biology Specialty Section

Other Endorser(s):
Drug Discovery Toxicology Specialty Section
Mechanisms Specialty Section

The genome and epigenome work hand-in-hand as central regulators of cell fate and function and, thus, serve as key mediators of susceptibility and toxic exposure effects. The use of traditional molecular methods has established a foundation with respect to the molecular mechanisms underlying the adverse effects of many toxic exposures; however, their efficacy in defining causative relationships between gene products, genetic polymorphisms, and epigenetic modification states with toxic exposure effects and susceptibility has been limited. The recent development of practical applications for clustered, regularly interspaced, short palindromic repeat (CRISPR), and Piwi-interacting RNA (piRNA) technology holds the potential to overcome these obstructions by permitting the selective revision of both the genome and epigenome in both toxicology research and clinical applications. CRISPR-mediated gene editing allows for the selective introduction or correction of mutations, deletion of target DNA, or introduction of fluorescent markers/biosensors or epitope tags to endogenous target genes or other loci. Further, piRNAs and deactivated CRISPR-associated protein 9 (dCas9) fusions with enzymes that add or remove epigenetic modifications can be targeted to alter both DNA methylation and histone modifications at specific loci to directly link changes in epigenetic modification states to exposure outcomes and susceptibility. The application of these technologies will open the door to the next generation of precision therapeutics and revolutionize the field of toxicology by providing novel opportunities to understand and modulate exposure-related disease and susceptibility at the genetic and epigenetic level. The goal of this session is to examine the range of applications of genome and epigenome engineering from their use in molecular and mechanistic toxicology studies to their potential as therapeutic strategies and to review the inherent safety considerations that their use entails. To achieve this, the session will bring experts together to discuss the development of these technologies and their current use in toxicity studies covering cultured human cells, mouse models, and human clinical trials. The session will answer questions such as: How do CRISPR-Cas9-mediated genomic/epigenomic engineering and piRNAs work, and what are the benefits and challenges facing their integration into the field of toxicology? Can CRISPR-Cas9 genomic editing be used to explore the role of key toxicity-associated pathways, such as NF-kB and NRF2, in the response to oxidative stress? How can the targeted modification of epigenetic states with dCas9 and piRNAs be used to provide causative relationships between specific epigenetic loci and disease/exposure outcomes? What is the current state of CRISPR-based therapies, and how does the toxicity and efficacy testing of these next-generation pharmaceuticals differ from that used for traditional therapeutic agents? The session will create a better understanding for the benefits, challenges, and applications of genome- and epigenome-engineering approaches in toxicology studies and will provide perspective on the unique considerations required during the development and testing of these technologies as next-generation therapeutic agents.

CRISPR and piRNAs: Fundamental Mechanisms and Key Applications of the Next Generation of Molecular Technologies in the Field of Toxicology. Shaun McCullough, US EPA, Chapel Hill, NC.

Use of CRISPR-Cas9 to Elucidate the Role of Nrf2 in the Response of T Cells to Electrophilic and Oxidative Stress. Cheryl Rockwell, Michigan State University, East Lansing, MI.

Applications of CRISPR-Cas9-Based Epigenetic Editing Technologies in Modeling and Treating Human Disease. Isaac Hilton, Duke University, Durham, NC.

Development of piRNAs for Target-Specific DNA Methylation. Dana Dolinoy, University of Michigan, Ann Arbor, MI.

Leading the Edge: Toxicity and Safety Testing with CRISPR-CAS-Based Therapeutics. Monika Chabicovsky, MC Toxicology Consulting GmbH, Vienna, Austria.

Regional Interest Session

Marijuana Safety: Issues Facing the Regulatory, Medical, and Academic Environments

Monday, March 12, 1:45 PM to 4:30 PM

Chairperson(s): *George Corcoran, Wayne State University, Detroit, MI; and Sol Bobst, ToxSci Advisors, Houston, TX.*

Primary Endorser:
Regulatory and Safety Evaluation Specialty Section

Other Endorser(s):
Clinical and Translational Toxicology Specialty Section
Ethical, Legal, Forensics, and Societal Issues Specialty Section

The presentations in this session will build upon a recent series of SOT Annual Meeting Roundtable and Workshop Sessions that broadly examined the legal applications and boundaries of toxicology and law. The 2016 Workshop Session "Cannabis in the Courtroom" explored topic areas for scientific testimony and briefly touched on the public health and safety impacts of legalized marijuana products. This session expands upon topics raised during the 2016 session which relate to the lack of federal oversight of the cannabis industry. With the growing acceptance of marijuana use and its legalization in some form (medical, recreational) by 28 states and the District of Columbia, including new medical marijuana legislation passed in Texas in 2017, marijuana has become a booming business that essentially is unregulated at the federal level because of the conflict imposed through listing of marijuana as a Schedule I drug by the Drug Enforcement Administration (DEA).

Texas has just passed medical marijuana laws in limited cases, opening up a new market for entrepreneurs in the state. Currently, the US government has relinquished authority to the states with respect to the growing, distributing, and selling of marijuana where it is legal to do so under state laws. This session will explore the impact of the current absence of federal oversight on public health and safety by presenting a number of scenarios and outcomes stemming from the widespread and legal uses of cannabis in more than half of the states and the stark differences in individual state regulations. Topics will include: 1) safety concerns for edible marijuana products; 2) regulatory status of marijuana and its implications for academic research; 3) policy implications for federal authorities in light of public perceptions of marijuana's benefits and risks; and 4) patient safety concerns with use of non-approved drug products and access to such products. The session will include a discussion from the legal perspective on the problems encountered with the "hands-off" approach currently taken by the federal government and will conclude with a panel discussion.

Marijuana and Public Safety Concerns: States in Charge. Laura Plunkett, Integrative Biostrategies LLC, Houston, TX.

Model Systems and Regulations for Cannabinoid Research in Academia. Barbara Kaplan, Mississippi State University, Starkville, MS.

Ensuring the Safety of "Edibles" in West Virginia: Lessons Learned for New Medical Marijuana Legislation in Texas. Erik Janus, Compassion West Virginia, Huntington, WV.

RMPC Colorado Marijuana Human Exposures by Age: 2014–2016. Chris Hoyte, Rocky Mountain Poison Control Center, Denver, CO.

Symposium Sessions

Clinical and Translational Toxicology: From Theory to Therapy

Tuesday, March 13, 8:00 AM to 10:45 AM

Chairperson(s): *Horst Thiermann, Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany; and Sally Bradberry, National Poisons Information Service (Birmingham Unit) and West Midlands Poisons Unit, Birmingham, United Kingdom.*

Primary Endorser:
Clinical and Translational Toxicology Specialty Section

Advancing the prevention and treatment of human toxicity is achieved only as a result of enthusiastic collaboration between scientists and clinicians from a wide range of disciplines. Together, they negotiate the painstaking, sometimes-tortuous path of translational toxicology—from bench to bedside, from theory to therapy. A better appreciation of the opportunities available to each discipline, as well as an improved understanding of the challenges and limitations each face, can enhance future collaboration and facilitate progress. This symposium will provide insight into the contemporary challenges and research opportunities encountered by toxicological experts from a wide range of disciplines, representing the laboratory, drug industry, and emergency room, as well as licensing and administration authorities, to inspire fruitful collaboration.

Introduction: The Translational Nature of Clinical Toxicology. John-Michael Sauer, Critical Path Institute, Tucson, AZ.

Restoration of Nerve Agent-Induced Paralysis of Human Respiratory Muscles *In Vivo*: How to Translate Results from *In Vitro* to the Clinic? Horst Thiermann, Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany.

Glutamate Dehydrogenase in Diagnosis of Liver Injury: A Biomarker Journey from Enabling Clinical Trials to Improving Medical Care. Jiri Aubrecht, Pfizer, Inc., Groton, CT.

From Bedside to Bench—What Only Our Patients Can Teach Us. Sally Bradberry, National Poisons Information Service (Birmingham Unit) and West Midlands Poisons Unit, Birmingham, United Kingdom.

Importance of Translation from *In Vitro* Testing to Approved Products and Treatments. Donna Mendrick, US FDA, Silver Spring, MD.

Summary of Clinical and Translational Toxicology: From Theory to Therapy. John-Michael Sauer, Critical Path Institute, Tucson, AZ.

Mitochondria Biogenesis and Dysfunction in Cellular Senescence in Cardiopulmonary System

Tuesday, March 13, 8:00 AM to 10:45 AM

Chairperson(s): *Irfan Rahman, University of Rochester, Rochester, NY; and James Wagner, Michigan State University, East Lansing, MI.*

Primary Endorser:
Inhalation and Respiratory Specialty Section

Other Endorser(s):
Cardiovascular Toxicology Specialty Section
Mechanisms Specialty Section

Emerging evidence sheds light on new mitochondrial functions that are not related to cellular energy production, which involve mitophagy (removal of damaged mitochondria from a cell prior to cell death) and mitochondrial protein quality control. Mitochondrial function is associated with fission, fusion, and mitophagy in health and disease. Mitochondrial proteins, such as Pink1, Parkin, and Drp1, along with sub-organellar signaling by oxidant stress and redox changes, are involved in mitochondrial dysfunction. This is associated with inflammation and cellular senescence via DNA damage and alterations in telomeric shelterin complex (a complex which protects telomeres from DNA damage). Toxicological perspectives on mitochondria or mitochondria toxicology (MitoTox) research include a multidisciplinary approach in different target organs in the pathogenesis of cardiopulmonary and vascular diseases. The goal of this session is to highlight the recent advances of mitochondria research in toxicology, particularly in mitochondria biogenesis, dysfunctional mitophagy, redox changes, cell signaling, and DNA damage/repair or rejuvenation of the damaged mitochondria upon toxic chemical or environmental insults in epithelial cells, fibroblasts, and myocytes in cellular senescence (premature aging) of the cardiopulmonary system. The information in the session will share the change in paradigm of involvement of mitochondrial stress signaling that would improve the gap in understanding the mechanisms of mitochondrial dysfunction in cellular senescence in the cardiopulmonary system.

Mitochondria-Nuclear Signaling and Mitophagy by Toxicants in DNA Damage and Lung Cellular Senescence. Irfan Rahman, University of Rochester, Rochester, NY.

Impairment of Mitochondrial Function by Particulate Matter and Nanometals in Cardiovascular and Pulmonary Diseases. John Hollander, West Virginia University School of Medicine, Morgantown, WV.

Cardiovascular Mitochondrial Dynamics and Dysfunction by Exposure to Ultrafine or Nano Particulate Matter. Christopher Wingard, Bellarmine University, Louisville, KY.

Mitochondrial DNA Damage and Dysfunction in Vascular Disease by Environmental Toxicants. Jessica Fetterman, Boston University School of Medicine, Boston, MA.

Redox Regulation of Mitochondrial Dysfunction and Cellular Senescence in Atherosclerosis. Reto Asmis, University of Texas Health Science Center at San Antonio, San Antonio, TX.

Workshop Sessions

Advancing the Adverse Outcome Pathway Framework: An International Horizon-Scanning Approach

Tuesday, March 13, 8:00 AM to 10:45 AM

Chairperson(s): *Rory Conolly, US EPA, Research Triangle Park, NC; and Markus Hecker, University of Saskatchewan, Saskatoon, SK, Canada.*

Primary Endorser:
Regulatory and Safety Evaluation Specialty Section

Other Endorser(s):
Biological Modeling Specialty Section
Risk Assessment Specialty Section

In 2007, the US National Research Council laid out a vision and strategy for toxicity testing in the 21st century, which aspired to transform current testing approaches by making greater use of recent scientific advances in cell-based and computational methods. The adverse outcome pathway (AOP) framework, which emerged to address this vision, has since gained international traction as a systematic approach for capturing existing knowledge to transparently link mechanistic data to apical toxicity endpoints as a means to inform research and risk assessment. While the framework has evolved significantly since its introduction in 2010, it was recognized that a survey of the broader scientific community would be useful in identifying challenges and in guiding future initiatives. To that end, a horizon-scanning exercise was conducted to solicit questions from the global scientific and regulatory communities, including the SOT community, concerning the perceived challenges and/or limitations that must be addressed to realize the full potential of the AOP framework in research and regulatory decision making. Questions submitted from all sectors and from across the globe were used to identify key themes that, if addressed, would significantly advance development and application of the AOP framework. Following this exercise, a Society of Environmental Toxicology and Chemistry (SETAC) Pellston™ Workshop, comprised of international participants representing industry, government, academia, and non-governmental organizations (NGOs), was held in Cornwall, Ontario, Canada, in April 2017 to begin exploring these themes and answering associated key questions. This session will serve as a podium to present the outcomes of the horizon-scanning exercise and of the Pellston™ Workshop and to foster discussion with attendees in order to continue advancing the AOP framework. Specifically, presentations will cover topics such as the development and application of AOP networks, quantitative AOPs and associated modeling approaches, and the status of and future needs for application of the framework in regulatory decision making. Furthermore, talks will explore a roadmap to enhance awareness of, involvement in, and acceptance of the AOP framework by regulatory agencies, scientists, and other stakeholder groups. Presentations will review frequently asked questions identified during the horizon scanning and address common misunderstandings pertaining to the AOP framework. Finally, the audience will be asked to participate in a panel discussion following the presentations to build upon ideas and outcomes derived from the Pellston™ Workshop.

Introduction. Rory Conolly, US EPA, Research Triangle Park, NC.

Adverse Outcome Pathways: Moving from a Scientific Concept to a Globally-Accepted Framework. Carlie LaLone, US EPA, Duluth, MN.

Adverse Outcome Pathway Networks: Development, Analytics, and Applications. Marie Fortin, Alcami, Edison, NJ.

How to Build and Apply Quantitative Models from Adverse Outcome Pathways. Edward J. Perkins, US Army Engineer Research and Development Center, Vicksburg, MS.

Using Adverse Outcome Pathways to Inform Decision Making for Chemical Innovation, Regulation, and Stewardship. Michelle Embry, ILSI Health and Environmental Sciences Institute (HESI), Washington, DC.

Making the AOP Framework Sustainable: Stakeholder Identification, Communication, and Engagement. Maurice Whelan, European Commission Joint Research Centre, Ispra, Italy.

Computational Predictions for Dermal Penetration of Chemicals: Should More Complexity Be Considered in Addition to Simple Passive Diffusion?

Tuesday, March 13, 8:00 AM to 10:45 AM

Chairperson(s): *Marina Evans, US EPA, Research Triangle Park, NC; and Ronald Baynes, North Carolina State University, Raleigh, NC.*

Primary Endorser:
Dermal Toxicology Specialty Section

Other Endorser(s):
Comparative and Veterinary Specialty Section

Risk assessment for thousands of chemicals, due to their potential exposure as environmental contaminants, is a daunting task. Because it is not feasible to obtain experimental data for this many chemicals, computational predictions have become part of the strategy for risk due to dermal penetration. An integrative modeling framework will become essential in this computational prediction strategy. While dermal exposure is a common mode of exposure, computational modeling for dermal penetration remains a challenging research area. This session will explore current approaches used to predict dermal penetration for chemicals with a wide spectrum of physical properties and applications. Some pharmaceutical products include dermal application of pesticides/insecticides. Consumer products include the additional challenge of consisting of mixtures and diverse combinations of vehicles with active ingredients. The physiology of the skin will be included into the computational predictions, including hydration, swelling, and additional components, such as nails or hair follicles. The impact of all these components will be discussed for inclusion in future dermal penetration predictions.

Computational Prediction of Dermal Diffusivity for Large Number of Chemicals: Challenges and Applications. Marina Evans, US EPA, Research Triangle Park, NC.

Skin Absorption of Metal Worker Fluids and Complexities Inherent in Additional Components. Ronald Baynes, North Carolina State University, Raleigh, NC.

Impact of Natural Compounds on Dermal Absorption for Consumer Products and Their Computational Prediction. James Riviere, North Carolina State University, Raleigh, NC.

The Skin Is a Non-Homogenous Physiological Organ—What Should We Consider for Computational Predictions? Gerald Kasting, University of Cincinnati, Cincinnati, OH.

***In Silico-In Vitro* Extrapolation for Dermal Exposure.** Jessica Spires, Simulations Plus, Lancaster, CA.

Defining Domains of Applicability for Zebrafish within Toxicology: A Retrospective and Prospective Workshop

Tuesday, March 13, 8:00 AM to 10:45 AM

Chairperson(s): *Jennifer Freeman, Purdue University, West Lafayette, IN; and David Volz, University of California Riverside, Riverside, CA.*

Primary Endorser:
Reproductive and Developmental Toxicology Specialty Section

Other Endorser(s):
***In Vitro* and Alternative Methods Specialty Section**
Molecular and Systems Biology Specialty Section

Over the past 20 years, adoption and integration of the application of zebrafish as a toxicological model system has magnified in most areas of toxicology-based research. As a well-recognized biomedical research model, zebrafish presents numerous strengths that have been leveraged in many toxicity studies. Rapid *ex vivo* development of a small, near-transparent singular embryo permits ease for assessing chemical perturbations at all stages of early development, as well as use in high-throughput chemical screens and automated phenotyping. In addition, a complete genome sequence, array of tools for manipulating gene function, and availability of several thousand mutant and transgenic lines provides, similarly to mouse models, readily available resources for comprehensive mechanistic studies of toxicity. Furthermore, maturation at three months of age and a shorter lifespan allow for multi- and transgenerational studies and efficient identification and evaluation of developmental origins of health and disease. As researchers continue to expand the use of the zebrafish in toxicology, limitations of this animal model also are being identified. In this session, the first presentation will highlight what has been learned from more than two decades of using zebrafish in toxicity research, which has spanned developmental mechanistic studies to current applications in high-throughput screening of chemicals and chemical mixtures. The second talk will discuss zebrafish as a comparative model to rodent neurobehavioral testing, including analysis of larval behavior outcomes with long-term neurobehavioral dysfunction in adults. The third speaker will focus on the advantages and challenges of using zebrafish to define mechanisms of immediate (larval), later in life (adult), and transgenerational consequences of a developmental toxicant exposure linking single-cell transcriptomic, epigenomic, and phenotypic outcomes. The fourth presentation will highlight the strengths and constraints for using transgenic zebrafish in drug development and therapeutics for epilepsy. The final speaker will address the benefits of using zebrafish as a replacement for mammalian toxicity testing and the importance of accounting for toxicokinetic processes and dosimetry. Overall, the session will bring together several leading research laboratories that have extensive experience with the zebrafish model in various toxicological disciplines to provide a reflection of the knowledge that has been gained over the past 20 years relative to the strengths and constraints of the model system in toxicological experiments. In addition, this session will explore a comparison of zebrafish to other animal models, best practices, current questions, and future research needs.

Introduction. Jennifer Freeman, Purdue University, West Lafayette, IN.

Utilizing the Power of High-Throughput Zebrafish Screening to Identify Hazardous Chemicals and to Help Design Safer Chemicals. Robert Tanguay, Oregon State University, Corvallis, OR.

Comparison of Larval and Adult Neurobehavioral Assays in Zebrafish after Toxicant Exposure during Early Development. Edward Levin, Duke University, Durham, NC.

Molecular Mechanisms for Persistence of the Effects of Developmental Toxicants: Using Zebrafish to Explore the Barker Hypothesis on the Fetal Basis of Adult Disease/Dysfunction and Their Potential for Transgenerational Inheritance. Michael Carvan, University of Wisconsin Milwaukee, Milwaukee, WI.

Exploring the Role of Toxicokinetics in the Response of Zebrafish Embryos and Larvae to Chemical Exposure. Kristin Schirmer, Eawag, Duebendorf, Switzerland.

Strengths and Constraints for Using Zebrafish for Epilepsy Drug Development. Kristine Willett, University of Mississippi, University, MS.

Get the Lead Out: The Persistent Problem of Lead Exposure from Soil, Dust, and Water

Tuesday, March 13, 8:00 AM to 10:45 AM

Chairperson(s): *Michael Hughes, US EPA, Research Triangle Park, NC; and Karen Bradham, US EPA, Research Triangle Park, NC.*

Primary Endorser:
Metals Specialty Section

Other Endorser(s):
Occupational and Public Health Specialty Section

The heavy metal lead, a known neurotoxicant, has been used for centuries in a variety of industries and household and consumer products. The choice to use lead is a reflection of its physical/chemical properties, including softness, ductility, poor conductibility, and resistance to corrosion. While a natural component of the Earth's crust, high concentrations of lead in the environment, particularly soil, have resulted from human activity and its resistance to natural degradation. From the decades-long use of lead as a fuel additive, soils in urban areas with high traffic volume have been found to have highly elevated levels of lead. In residences that pre-date 1978, when lead-based paint was banned in the United States, dust from deteriorating paint contains elevated levels of lead. The soils on and near several industrial smelting sites, such as in East Chicago, IN, also have high levels of lead. Finally, lead is found in drinking water in homes that have water pipes containing lead, with leaching a complex function of pH, alkalinity, and source water characteristics. It is well-noted that homes typically located in older urban centers have drinking water with a high risk of elevated lead levels, particularly if the water is corrosive. Elevated blood levels have been found in people, particularly children, who were exposed to soils, dust, and water containing high levels of lead. The main public health issue with lead is that it is neurotoxic, especially to children. Elevated levels of lead in children can result in behavioral disorders and impairment of intelligence and learning. There is no known biological requirement for lead, although it is absorbed fairly well following ingestion or inhalation. Lead accumulates in bone, as it has similar properties as calcium, taking its place in this organ. Lead in bone can be a long-term source of internal exposure, as it can be released from bone into the systemic circulation and distributed to other organs. This session will bring together experts on lead with regard to its exposure, neurotoxicological effects, and the use of models to predict blood lead levels in individuals exposed to lead in soil, dusts, and water. The first presenter will discuss the positive association

between lead in soil or bioaccessible (an *in vitro* method simulating the gastrointestinal tract) lead and blood lead levels in children in an urban area. This presentation will show the feasibility of using *in vitro* methods to improve child lead risk assessments in the place of total soil lead content. The second presentation will share how soil lead levels and children's blood levels have changed pre- and 10 years post-Hurricane Katrina in New Orleans, Louisiana. It was observed that with decreased soil lead levels after hurricane, the blood lead levels in the children also decreased. The third presentation will focus on the potential mechanisms of lead that result in adverse health outcomes following maternal lead exposure with the potential development of neurotoxicity in the offspring. This includes studies from both human and laboratory animal maternal exposures. The fourth presentation will evaluate the impact of varying regional screening levels on blood lead predictions in the Integrated Exposure Uptake Biokinetic (IEUBK) model to aid in reducing uncertainty in human health risk assessments. The final presentation will describe the application of the US Environmental Protection Agency's (US EPA) SHEDS-Multimedia and IEUBK models to determine the level of lead in drinking water that should result in children's blood lead levels that are less than specified values. The analysis reveals the importance of the soil and dust ingestion exposure pathway. The session will share information on the association between exposure to lead in soils, dusts, and water to blood lead levels, neurotoxic mechanisms of lead exposure, and modeling efforts to predict children's blood lead levels following exposure. *Disclaimer: The views expressed are those of the authors and do not necessarily represent the views or policies of the US EPA.*

Bioaccessibility of Lead in Urban Residential Philadelphia Soils. Karen Bradham, US EPA, Research Triangle Park, NC.

The Astonishingly Holistic Role of Soil in Lead Exposure of Children. Howard Mielke, Tulane University School of Medicine, New Orleans, LA.

Lead-Induced Neurotoxicities: From Maternal Exposure to Neurodegenerative Alzheimer's Disease. Wei Zheng, Purdue University, West Lafayette, IN.

Evaluating the Impact of Alternate Assumptions on Soil Remedial Levels Using EPA's Integrated Exposure Uptake Biokinetic (IEUBK) Model. Barbara Beck, Gradient, Cambridge, MA.

Probabilistic Modeling of Childhood Multimedia Lead Exposures: Examining the Soil Ingestion Pathway. Rogelio Tornero-Velez, US EPA, Research Triangle Park, NC.

Nanotoxicology: State of the Science and the Path Forward

Tuesday, March 13, 8:00 AM to 10:45 AM

Chairperson(s): *Treye Thomas, US Consumer Product Safety Commission, Rockville, MD; and Aaron Erdely, NIOSH, Morgantown, WV.*

Primary Endorser:
Nanotoxicology Specialty Section

The US National Nanotechnology Initiative (NNI) was established in 2001 to support the responsible development of the emerging science of nanotechnology and bring together stakeholders from the federal government, industry, and academia. The goal was to thoroughly address the potential health and safety implications of nanomaterials. Stakeholders emphasized the complexity of nanotoxicology, the importance of understanding the novel physicochemical properties of nanomaterials, and how traditional toxicity testing strategies should be modified to address these unique properties. The toxicology community has responded to this call-to-action through the emergence of nanotoxicology as a subspecialty, including the 2008 launch of the SOT Nanotoxicology Specialty Section. Over the past 10 years, thousands of peer-reviewed studies have been published in journals, including those developed specifically for nanotoxicology, in addition to numerous meetings and symposia. Currently, the nanotoxicology community is at a critical juncture where stakeholders have begun to pose serious questions regarding the achievements of this new science. Concerns include the presentation and robustness of the data in published studies and whether standardized and validated methods were used. General questions surround whether available data meet critical data gaps, whether nanotoxicology should continue to exist as a subdiscipline of toxicology, and whether funding should be consolidated. The toxicology community should work in tandem with other disciplines that play a critical role in understanding the relative risks associated with nanomaterials. This session will bring together researchers and scientists from the federal government, industry, and academia to provide an overview of the lessons learned and the support provided to industry for commercializing nano-enabled products. The session will present carbon nanotube toxicity as a case study of the efforts to understand whether toxicity of engineered nanomaterial exposures is adequately understood. Other topics include the state of the science in terms of human health effects, the role of the NNI in assuring responsible development of nanotechnology, and the future directions of industries for incorporating nanotechnology. Lastly, the path forward for nanotoxicology, highlighting knowledge gaps and emerging research needs, will be presented, followed by an open discussion with the panel of speakers.

Introduction. Treye Thomas, US Consumer Product Safety Commission, Rockville, MD.

State of the Science: Nanotoxicology of Carbon Nanotubes (CNTs). Vincent Castranova, West Virginia University, Morgantown, WV.

State of the Science: Human Health Effects of Engineered Nanomaterials. Mary Schubauer-Berigan, NIOSH, Cincinnati, OH.

Ensuring Responsible Development of Nanotechnology. Lisa Friedersdorf, National Nanotechnology Coordination Office (NNCO), Arlington, VA.

An Industry Perspective on the Federal Role in Nanotoxicology. Shaun Clancy, Evonik, Parsippany, NJ.

Nanotoxicology and the Path Forward. Alison Elder, University of Rochester, Rochester, NY.

Panel Discussion. Charles Geraci, NIOSH, Cincinnati, OH; and Sally Tinkle, Science and Technology Policy Institute, Washington, DC.

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See page 5 for details regarding session types and lengths.

Roundtable Session

Alternative Toxicology Approaches to Evaluate Next-Generation Nicotine Products

Tuesday, March 13, 11:00 AM to 12:20 PM

Chairperson(s): *John Fowle III, Science to Inform, LLC, Pittsboro, NC; and Erin Hill, Institute for In Vitro Sciences, Gaithersburg, MD.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

Other Endorser(s):
Inhalation and Respiratory Specialty Section
Risk Assessment Specialty Section

The development and uptake of novel nicotine products, including e-cigarettes, has grown rapidly around the world in the last decade, creating a need to evaluate the potential health risks associated with the use of these products. The US Food and Drug Administration Center for Tobacco Products and the European Union Tobacco Products Directive have made recommendations and issued guidance documents outlining the criteria for assessing the risks of these novel products. As part of these proposed frameworks, significant nonclinical testing is required. A wide variety of stakeholders are concerned about the large number of animals that potentially could be used for testing. This roundtable will explore the opportunities and challenges in utilizing *in vitro* and other alternative toxicology testing methods for the assessment of e-cigarettes. The panel members, representing a wide range of viewpoints, including academia, industry, and government, will discuss: 1) how global regulations are impacting research; 2) what innovations are necessary to make the science ready for regulatory decision making; 3) how to foster collaboration to ensure standardization of approaches; 4) what lessons can be taken from other industries and agencies adopting alternative approaches; 5) what role industry and other stakeholders can play; and 6) how progress can be accelerated.

Alternative Toxicology Approaches to Evaluate Next-Generation Nicotine Products. John Fowle III, Science to Inform, LLC, Pittsboro, NC.

A Roadmap to Establishing New Approaches for Toxicity Testing: Improving Human Relevance and Reducing Animal Use. Warren Casey, NIEHS, Research Triangle Park, NC.

E-Cigarettes: The Lesser Evil or the Public Health Opportunity of the 21st Century? Thomas Hartung, Johns Hopkins Center for Alternatives to Animal Testing, Baltimore, MD.

Successful Collaborations between Industry and Regulators. Erin Hill, Institute for In Vitro Sciences, Gaithersburg, MD.

Alternative Toxicology Approaches for the Evaluation of Next-Generation Nicotine Products: Manufacturer's Perspective. Christopher Proctor, British American Tobacco, London, United Kingdom.

Historical Highlights Session

Arsenic, a Gift and Malice: From Discovery to Detrimental Effects, a Historical Perspective

Tuesday, March 13, 11:00 AM to 12:20 PM

Chairperson(s): *Brinda Mahadevan, Abbott Laboratories, Mumbai, India; and Madhu Soni, Soni & Associates, Inc., Vero Beach, FL.*

Primary Endorser:
Metals Specialty Section

Other Endorser(s):
Association of Scientists of Indian Origin Special Interest Group
Food Safety Specialty Section

From natural/industrial toxin to chemical warfare, murder to crime fiction, healer to poison, arsenic remains a powerful force in modern life. Arsenic toxicity is a global health problem affecting millions of people. Apart from the limit on levels of arsenic (10 parts per billion (ppb)) in drinking water established by the US Environmental Protection Agency, the US Food and Drug Administration (US FDA) has been measuring total arsenic concentration in foods through its Total Diet Study and has come up with limit levels. In order to better understand the toxicity of arsenic, one needs to consider arsenic speciation, which includes inorganic arsenic (As III, As V, and total), as well as organic arsenic (dimethylarsenic acid and monomethylarsenic acid). The US FDA found that inorganic arsenic exposure in infants and pregnant women can result in a child's decreased performance on certain developmental tests that measure learning based in epidemiological evidence about arsenic, including dietary exposure. More recently, the US FDA has proposed an "action level" of 10 ppb for inorganic arsenic in apple juice. The objectives of this symposium are to provide: 1) historical and scientific understanding of arsenic from toxicology and therapeutic perspective; 2) safety policies; 3) recent updates on mechanism of arsenic toxicity and carcinogenesis; and 4) the thought process on arsenic exposure through food.

Introduction to Millennial Use of Arsenic and Toxicological Effects. Madhu Soni, Soni & Associates, Inc., Vero Beach, FL.

A Historical Perspective on the Dichotomy of Arsenic as a Poison and Medicinal Agent. Michael Hughes, US EPA, Research Triangle Park, NC.

Arsenic Carcinogenesis. Samuel Cohen, University of Nebraska Medical Center, Omaha, NE.

The Daunting Task of Looking for Arsenic in Foods: An FDA Perspective. Suzanne Fitzpatrick, US FDA, College Park, MD.

Education-Career Development Session

In It to Win It: How to Negotiate During the Interview Process

Tuesday, March 13, 11:00 AM to 12:20 PM

Chairperson(s): *Karilyn Sant, University of Massachusetts, Amherst, MA; and Cynthia Browning, Brown University, Providence, RI.*

Primary Endorser:
Postdoctoral Assembly

Other Endorser(s):
Career Resource and Development Committee
Graduate Student Leadership Committee

After years of professional training, early-career toxicologists are eager to start interviewing to finally secure their dream job. While nailing the interview is important, navigating the delicate process of negotiations is critical to successfully sealing the deal. However, negotiations are often kept private, giving trainees little knowledge of negotiation logistics and etiquette. Further, negotiating procedure and tactics can vary widely between academia, industry, and government. This session is designed to provide trainees with tips and strategies that will help them successfully navigate the negotiation process. Speakers, representing successful toxicologists from academia, industry, and government, will: 1) provide an overview of the negotiation process; 2) give advice on specific items that are included in recruitment packages; and 3) present practical examples of negotiating skills and techniques. The presentations will be interactive and will engage the audience through live polling technology, role playing, and mock negotiations. These discussions will be highly relevant to all student and postdoctoral attendees, as well as senior toxicologists considering a transition across the professional sectors. This career development session will stimulate an active discussion about how negotiations proceed and provide trainees with strategies, tips, and the confidence to navigate this daunting process and secure their dream job.

Strategies for Negotiating Both Salary Compensation and Start-Up Package to Assure Productivity and Success in Your First Academic Job at a Research-Intensive Institution. John Richburg, University of Texas, Austin, TX.

Getting to Yes: Academic Negotiations at a Primarily Undergraduate Institution. Larissa Williams, Bates College, Lewiston, ME.

The Art of Interviewing and Negotiating for Your First Post-Training Job in the Pharmaceutical Industry. Joseph Cichocki, Alnylam Pharmaceuticals, Cambridge, MA.

There's Usually No Harm in Asking. Marie Fortin, Alcami Corporation, Wilmington, NC.

Negotiating with the Federal Government: What's Actually on the Table? Tamara Tal, US EPA, Research Triangle Park, NC.

Symposium Sessions

Application of Data from New Approaches in Regulatory and Product Safety Decisions

Tuesday, March 13, 1:30 PM to 4:15 PM

Chairperson(s): *Russell Thomas, US EPA, Research Triangle Park, NC; and Mike Rasenberg, European Chemicals Agency (ECHA), Helsinki, Finland.*

Primary Endorser:
Regulatory and Safety Evaluation Specialty Section

Other Endorser(s):
***In Vitro* and Alternative Methods Specialty Section**
Risk Assessment Specialty Section

Following more than 10 years of evolution in applied toxicology from the release of the seminal National Research Council report *Toxicity Testing in the 21st Century: A Vision and a Strategy* and the progress-to-date highlighted in the 2017 report, *Using 21st Century Science to Improve Risk-Related Evaluations*, there is now broad recognition of the problem to be targeted with innovations in applied toxicology: Hazard and exposure assessments are needed for thousands of chemicals, and the data gaps present cannot be filled using solely traditional methods in toxicology and exposure science due to time and resources. High-throughput predictions for bioactivity and exposure are beginning to inform both regulatory and product safety decisions, including prioritization, screening-level assessments for emerging contaminants, read-across, and product development and safety assessment decisions. Critical to the use of high-throughput and alternative methods for decisions informed by toxicology is definition of the qualitative and quantitative uncertainty of these methods to ensure conservative protection of human and ecological health. The purpose of this symposium is to provide details on successful first implementations using high-throughput toxicology tools in specific types of decisions and how the associated uncertainty with these tools was understood and accounted for within the decision. Importantly, the lessons learned from these early applications of high-throughput methods to regulatory and product safety decisions will provide the context for modification of high-throughput tools and data interpretation to meet the ongoing challenges of more rapid and efficient safety assessments.

Application to Prioritization for Health Canada's CMP.
Tara Barton-MacLaren, Health Canada, Toronto, ON, Canada.

GenRA: From Research and Implementation to Practical Application.
Grace Patlewicz, US EPA, Research Triangle Park, NC.

Utilizing Novel Data Streams to Characterize Emerging Contaminants in the Superfund Program. Alicia Frame, US EPA, Arlington, VA.

Utilization of High-Throughput Data for Product Safety Assessment.
Reza Rasoulpour, Dow AgroSciences, Indianapolis, IN.

Application to Risk Assessment: Can Bioactivity Predictions Be Used as a Conservative Point-of-Departure? Katie Paul Friedman, US EPA, Research Triangle Park, NC.

Effectively Leveraging Cellular Functional Genomics Strategies for Elucidating Chemical Mechanisms of Action

Tuesday, March 13, 1:30 PM to 4:15 PM

Chairperson(s): *Audrey Bone, US EPA, Research Triangle Park, NC; and Federica Piccioni, Broad Institute of MIT and Harvard, Cambridge, MA.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

Other Endorser(s):
Mechanisms Specialty Section
Molecular and Systems Biology Specialty Section

High-throughput toxicity testing has become increasingly important in the field of toxicology, as evidenced by the advent of programs such as Tox21 and ToxCast. However, these programs cover a fairly limited amount of biological space and are constrained by current knowledge of biological pathways of toxicity. In order to comprehensively assess the potential for chemical hazard without the bias of only investigating known pathways, more wide-ranging screening techniques are needed. In recent years, new technologies have been developed that broadly can be referred to as functional genomics (or proteomics), which are capable of globally determining genes/gene products that are critically involved in chemical interactions. Techniques include, but are not limited, to: 1) yeast knockout collection with haploinsufficiency profiling/homozygous deletion profiling (HIP/HOP) technology and the like, which uses chemical tolerance or intolerance to identify toxicity targets; 2) CRISPR-Cas9 knockout screening in human cells, which functions similarly to the HIP/HOP screen; 3) proteomics methods that identify specific chemical-protein interactions in the context of the entire cellular milieu; and 4) transcriptomics methods which use the technologies of next-generation sequencing (NGS) to study the cellular state of healthy, chemically perturbed, and/or diseased tissue. These techniques cover more comprehensive biological space that may provide data leading to discovery of new biological targets and pathways of toxicity. In addition, since these techniques provide some measure of cell health as a result of gene manipulation linked to chemical insult, the role of each gene in either chemical tolerance or intolerance can be functionally ascertained. The purpose of this session is to provide an overview of the cell-based techniques that are currently in use or being developed to demonstrate powerful new ways of determining mechanisms of toxicity for environmental and other chemicals. One of the co-chairs will provide an introductory overview of functional genomics and describe how these technologies could be applied in 21st-century toxicology. The first speaker will describe the use of a large panel of diverse cell types, including cell lines, iPSC and primary cells, with critical gene targets modified using CRISPR-Cas9 technology to identify critical chemical targets. Validation of results using both CRISPRi (inactivation) and CRISPRa (activation) of targets identified also will be demonstrated and use of these approaches in understanding off-target effects of drugs. The second speaker will discuss the use of CRISPR technology to identify genes following arsenic exposure that promote the endoplasmic reticulum stress response and apoptosis in human cells. Experimental data presented will include novel validated gene hits, in particular, those of the polycomb repressive complex and microRNAs. The third speaker will continue the discussion of the use of CRISPR technology in human cells for functional genomics by presenting work done in human erythroleukemic K562 cells exposed to arsenic trioxide or acetaldehyde. The speaker will present data that demonstrates not only the utility of this approach to identify novel toxicity pathways, as he will show in the case of arsenic trioxide, but also the capability to assign potential roles to uncharacterized proteins based on known toxicity pathways, as he will show in the case of acetaldehyde and DNA repair. The fourth speaker will compare use of gain of function and loss of function genomic screens using lentivirus to deliver an open reading frame library into human cells to characterize mechanisms of action of drugs in cancer cell lines and compare this approach to CRISP-Cas9 methods. The final speaker will discuss an unbiased chemical proteomics platform that identifies chemical-protein interactions in intact cells by a variety of techniques such as target identification by ligand stabilization. Applications of the methods will be provided, such as identification of the target of a brominated flame retardant. The material in this session will demonstrate how functional genomics techniques have the potential to address a major gap in current toxicological paradigms. Determining chemical mechanisms of toxicity are currently limited by incomplete knowledge of biology. Functional genomics techniques provide an opportunity to develop high-throughput toxicity testing with the advantage of covering a more complete biological space and a functional measure of toxicity. *Disclaimer: The views expressed are those of the authors and do not necessarily represent the views or policies of the US Environmental Protection Agency.*

Filling in the Gaps: The Role Functional Genomics Can Play in 21st-Century Toxicology. Audrey Bone, US EPA, Research Triangle Park, NC.

The Use of CRISPR-Cas9 Technology for Validation and De-Validation of Targets from Functional Genomics. Lorenz Mayr, AstraZeneca, Cambridge, United Kingdom.

CRISPR Genetic Screens on Cellular Stress Response to Proteo-Toxicants. Quan Lu, Harvard T.H. Chan School of Public Health, Boston, MA.

Genome-Wide CRISPR-Cas9 Screens in Human Cell Lines Provide Novel Mechanistic Insights into Toxic Responses to Arsenic and Acetaldehyde. Amin Sobh, University of California Berkeley, Berkeley, CA.

Pooled Genome-Wide Screens as a Powerful Tool for Studying Drug Mechanism of Action in Cancer. Federica Piccioni, Broad Institute of MIT and Harvard, Cambridge, MA.

Development of a Hybrid Chemical Proteomics Platform for Proteome-Wide Identification of Protein Targets of Environmental Chemicals. Hui Peng, University of Toronto, Toronto, ON, Canada.

ITS Stressors from Within: Neuroendocrine Regulation of Air Pollution-Induced Pulmonary and Systemic Health Effects

Tuesday, March 13, 1:30 PM to 4:15 PM

Chairperson(s): *Urmila Kodavanti, US EPA, Durham, NC; and Samantha Snow, US EPA, Durham, NC.*

Primary Endorser:
Inhalation and Respiratory Specialty Section

Other Endorser(s):
Women in Toxicology Special Interest Group

Air pollution research has traditionally focused on exploring the mechanisms linking acute and chronic exposure to lung injury/inflammation and, ultimately, the development and exacerbation of airway diseases. More recently, evidence has emerged linking air pollution to adverse cardiovascular health effects, neurological diseases, systemic inflammation, diabetes, obesity, steatohepatitis, and poor reproductive and developmental outcomes. A novel paradigm has been proposed involving the role of central nervous system activation to explain pulmonary and extra-pulmonary effects of inhaled pollutants. The new evidence in general brings forth a compelling common mechanism involving sympathetic-adrenomedullary and hypothalamus-pituitary-adrenal axes-mediated systemic homeostatic stress responses that can explain the widespread multi-organ metabolic and immune effects of air pollution. The role of these neuroendocrine axes in mediating systemic effects of pollutants has been overlooked in the past. This mechanism emphasizes the importance of considering a systems biology approach for inhaled pollutants and other stressors and proposes a common mechanistic pathway for chemical and non-chemical stressors. The unifying hypothesis involving the neuroendocrine axes will be presented and supported by each speaker to specifically explore: 1) the basic understanding of how acute physical and psychological stresses (good stress) through neuroendocrine activation mediate immune cell egress and extravasation and other homeostatic changes and, in the long term, contribute to chronic inflammatory diseases (bad stress); 2) epidemiological evidence linking environmental stressors, specifically air pollutants, to the neuroendocrine pathway leading to exacerbation of inflammatory conditions of asthma and chronic obstructive pulmonary disease (COPD), which will include looking at the interactive effects of psychological and environmental stressors during development and susceptibility to chronic respiratory diseases; 3) how irritant pollutants likely activate neuroendocrine stress response through nociception by stimulation of sensory nerves, including vagal C-fibers, and integrate sensory signals to the brain to stimulate stress-responsive centers including hypothalamus, which is involved in a flight-or-fight response upon physical stress encounter; 4) experimental studies examining how exposure to inhaled pollutants through neuroendocrine stress response pathways activate adrenergic and steroidal mechanisms and alter systemic metabolic homeostasis to affect liver, muscle, and adipose tissue lipid and glucose metabolism and influence lung injury/inflammation; and 5) the development of a glucocorticoid receptor adverse outcome pathway to integrate the new mechanistic information on environmental sensory irritants and metabolic and immune dysfunction through neuroendocrine stress axes activation and tissue-specific activation of stress hormone receptors. The goal of this session is to synthesize and discuss these emerging findings in order to build a consensus that neuroendocrine stress axes play a major role in air pollutant and environmental health effects and disease susceptibility. The topics covered also will highlight areas where redirection of research efforts might better address the most critical knowledge gaps in the understanding of air pollutant-induced modulation of neuroendocrine pathways and disease susceptibility and improve health risk assessment.

Neuroendocrine-Immune Effects of Stress in Health and Disease. Firdaus Dhabhar, University of Miami Miller School of Medicine, Miami, FL.

Role of Social and Physical Stressors in Programming of Chronic Lung Diseases and Therapeutic Interventions. Rosalind Wright, Icahn School of Medicine at Mount Sinai, New York, NY.

Autonomic Regulation of Systemic Health Effects of Air Pollution: The Role of Sensory Stimulation. Thomas Taylor-Clark, University of South Florida, Tampa, FL.

Air Pollution and Neuroendocrine Stress-Mediated Systemic Metabolic and Inflammatory Response. Urmila Kodavanti, US EPA, Durham, NC.

Adverse Outcome Pathway Network of Adrenergic and Glucocorticoid Signaling Links Inhaled Pollutants with Multiple Adverse Outcomes. Stephen Edwards, US EPA, Durham, NC.

WORKSHOP SESSIONS

Big Data in Toxicology: How to Achieve Transparency and Reproducibility

Tuesday, March 13, 1:30 PM to 4:15 PM

Chairperson(s): *Agnes Karmaus, ILS, Research Triangle Park, NC; and Lyle Burgoon, US Army Engineer Research and Development Center, Research Triangle Park, NC.*

Primary Endorser:
Ethical, Legal, Forensics, and Societal Issues Specialty Section

Other Endorser(s):
***In Vitro* and Alternative Methods Specialty Section**
Regulatory and Safety Evaluation Specialty Section

You have performed your experiment or analysis, generated or used toxicological big data, want to publish it, and need it to be transparent and reproducible. What do you do? This is one of the challenges faced when using or generating toxicological big data (high-throughput screening, high-content assays, or 'omics technologies). Data analyses have become more complex, with increasing scrutiny being placed on the computational methods to ensure analyses are clearly communicated (transparency) and easily reproduced. Supplementary data files may be insufficient to adequately relay the necessary detail or metadata, nor meet the data quality needs and minimum information criteria required for risk assessors to utilize such data/analyses. This session seeks to address these challenges facing toxicologists highlighting platforms for data sharing, how to cite alternative data sources, and the minimum information required for reproducibility and transparency that will help lead toward regulatory acceptance of big data. Furthermore, in order for complex models to be broadly utilized and reproducible, and clear methodologies, as well as developing fit-for-purpose models that address specific needs, are required. This session will encompass various viewpoints—from the research perspective to that of regulators and industry—providing suggestions and resources for establishing reliable and useful models, as well as promoting transparent communication regarding the use of big data and computational approaches in the toxicological sciences. An aim of the session is to promote awareness regarding the dissemination and use of big data in toxicology, and it will conclude with a panel discussion including all speakers.

Introduction. Agnes Karmaus, ILS, Research Triangle Park, NC.

Challenges Facing Publication and Transparency for Big Data in Toxicology. Lyle Burgoon, US Army Engineer Research and Development Center, Research Triangle Park, NC.

Big Data in Toxicology: Remodeling the Publishing Landscape. Gary W. Miller, Emory University, Atlanta, GA.

Resources and Alternative Publication Streams for Big Data. Antony Williams, US EPA, Research Triangle Park, NC.

Utility of Big Data: Developing Reliable Fit-for-Purpose Data Models. Matthew Martin, Pfizer, Inc., Groton, CT.

Establishing Confidence in Prediction Models. Lars Carlsson, AstraZeneca, Mölndal, Sweden.

Mitochondria: Critical Targets in Pharmaceutical and Environmental Toxicity

Tuesday, March 13, 1:30 PM to 4:15 PM

Chairperson(s): *Bob van de Water, Universiteit Leiden, Leiden, Netherlands; and Yvonne Will, Pfizer, Inc., Groton, CT.*

Primary Endorser:
Drug Discovery Toxicology Specialty Section

Other Endorser(s):
Molecular and Systems Biology Specialty Section

Mitochondria are essential for cellular metabolism, and mitochondrial damage is a key event in adverse outcome pathways. Toxic insults causing mitochondrial dysfunction can lead to cellular necrosis due to loss of adenosine triphosphate production, to apoptosis through cytochrome-C leakage, and to many other adverse events, including reactive oxygen species production. Speakers from academia and industry will discuss several aspects of mitochondrial toxicity in the context of pharmaceutical and environmental toxicity. The goal is to present current insights into the central role of mitochondria in distinct toxicity pathways and state-of-the-art approaches to investigating mitochondrial toxicity. The latest technologies, including transcriptomics, proteomics, and metabolomics, as well as fluorescent protein reporters in combination with high-resolution microscopy, provide time-resolved mechanistic insight into cause and consequences of chemical-induced mitochondrial injury. The session will start with cutting edge work that centers on the mechanisms by which mitochondrial quality is maintained and how damaged mitochondria are removed from the cell. This will be followed by new findings obtained through metabolomic characterization of isolated human mitochondria and definition of the mitochondrial exposome. The next presentation will feature exciting work showing how off-target adverse drug effects on mitochondrial energetics cause muscle dysfunction. The following presenter will discuss innovative approaches to unraveling mitochondrial toxicity pathways as developed in the EU-ToxRisk project. The final presenter will address how changes in mitochondrial biogenesis serve as a cellular adaptive mechanism counteracting drug-induced liver toxicity. This session will be of general interest to scientists interested in cellular and tissue-level mechanisms of toxicity. In addition, attendees with an interest in state-of-the-art approaches to unraveling pathways of toxicity in a time- and concentration-resolved manner will benefit from the session. Finally, this session will be of interest to regulatory scientists incorporating information from *in vitro* assays in the decision-making process.

Introduction. Bob van de Water, Universiteit Leiden, Leiden, Netherlands.

New Insights in Mitochondrial Quality Control and Mitophagy. Åsa Gustafsson, University of California San Diego, San Diego, CA.

The Mitochondrial Exposome. Douglas Walker, Emory University, Atlanta, GA.

Drug-Induced Myopathy through Adverse Effects on Mitochondrial Energetics. Frans Russel, RIMLS, Amsterdam, Netherlands.

EU-ToxRisk: Advances in High-Content Microscopy Analysis for Mitochondrial Toxicity. Erik Danen, Universiteit Leiden, Leiden, Netherlands.

Increased Mitochondrial Biogenesis as a Cellular Adaptive Mechanism Counteracting Drug-Induced Liver Toxicity. Paul Carmichael, Unilever, Sharnbrook, United Kingdom.

Safety Evaluation of Plant-Based Color Additives Used in Foods

Tuesday, March 13, 1:30 to 4:15 PM

Chairperson(s): *Yu (Janet) Zang, US FDA, College Park, MD; and Maria Bastaki, International Association of Color Manufacturers (IACM), Washington, DC.*

Primary Endorser:
Food Safety Specialty Section

Other Endorser(s):
Mixtures Specialty Section
Regulatory and Safety Evaluation Specialty Section

Color plays a significant role in food choice by influencing consumer preference, taste perception, and acceptability. With an increasing number of consumers looking for foods with "clean labels," the market demand for "natural" colors has recently been rising significantly. There have been a growing number of food manufacturers turning away from synthetic colors and towards extracts from plant sources, primarily because of the increasing public interest in "natural" products. Currently, global regulatory agencies do not have a harmonized viewpoint as to the definition of color additives from botanical sources and their use requirements. In the United States, any unapproved color additive from a natural source is subject to premarket safety review by the US Food and Drug Administration (US FDA) with the same safety standard as for synthetic color additives. For plant-based color additives, considerations include chemical identity and composition, manufacturing process, source plant material, heat, pH, light stability, and pesticide and toxic element contamination. In the European Union, a decision tree is used to help determine when an ingredient can be considered a coloring food versus a coloring additive, with the latter being subject to scientific safety assessment. Failure to be aware of the regulatory review requirements can lead to compliance and labeling challenges and possibly charges of adulteration and misbranding upon importation of finished food items. Dialogues and collaborations among stakeholders, including color manufacturers, industrial end users, researchers, and regulatory scientists, are needed.

They should work together to harmonize and optimize the safety evaluation of plant-based color additives. This workshop brings together food color experts from these stakeholder groups to share their experiences and perspectives on this topic. Following an introduction that will summarize the use pattern of food colors, speakers will discuss wide-ranging topics related to the safety evaluation of plant-based color additives used in foods, including: 1) the differences between synthetic and natural color with regard to manufacturing and practical applications; 2) segments along the supply chain and manufacturing process impacting the safe use of these colors; 3) issues with product quality related to adulteration and contamination that compromise the safety; 4) United States Pharmacopeia (USP)'s experiences in establishing identity and specification standards for plant extracts; 5) the US FDA review process and special considerations; and 6) highlights of the most recent developments by global regulatory authorities. Examples of data packages sent to the US FDA, European Food Safety Authority (EFSA), and the Joint Food and Agricultural Organization of the United States (FAO)/World Health Organization (WHO) Expert Committee on Food Additives to support safety will be presented.

The Safe Use of Plant-Based Color Additives: An Introduction. Maria Bastaki, International Association of Color Manufacturers (IACM), Washington, DC.

Safety Considerations in Using Natural Color Additives: Industry's Perspectives. George Pugh Jr., The Coca-Cola Company, Atlanta, GA.

Coloring and Co-Existing Ingredients in Plants Used to Dye Foods. Stephen Talcott, Texas A&M University, College Station, TX.

Establishing Standards for Natural Extracts: Experiences from USP. Hellen Oketch-Rabah, United States Pharmacopeia (USP), Rockville, MD.

Assessing the Safety of Plant-Based Food Colors in a Regulatory Setting. Yu (Janet) Zang, US FDA, College Park, MD.

Global Regulations for Plant-Based Food Colors. Sue Ann McAvoy, Sensient Colors LLC, St. Louis, MO.

Regional Interest Session

Communicating Science: Unconventional Oil and Gas Operations as a Case Study

Tuesday, March 13, 1:30 PM to 4:15 PM

Chairperson(s): *David Steup, Shell Oil Company (Retired), Houston, TX; and Erica Bruce, Baylor University, Waco, TX.*

Primary Endorser:
Lone Star Regional Chapter

Other Endorser(s):
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Ten years ago, there was a rapid increase in oil and natural gas development activities (OGD) in various unconventional resource basins around the country. The increase was the result of an innovative use of existing technologies (horizontal drilling and hydraulic fracturing). The transformation also led to a rapid increase in the build out of the infrastructure required to deliver the product to the markets (i.e., pipelines, compressor stations) and facilities for processing the product (i.e., natural gas process facilities, liquefaction facilities). While the increase was a boon to the economy, it also generated scrutiny from policymakers, researchers, and advocates who commonly cited health concerns. As the decade mark of the nationwide ramp up in industry operations and activities approaches, some of the same challenges still exist. One of the aspects of addressing health concerns might be to align risk perceptions with the actual risks related to OGD and infrastructure development activities. Texas has a rich history of OGD going back to the early 20th century and is home to some of the largest shale basins (the Permian Basin, Eagle Ford Shale, and Barnett Shale) in the United States. Industry activities are a critical part of the Texas economy, and despite the challenges, Texas has managed to maintain these activities while addressing the growing environmental and health concerns.

Toxicological principles and toxicologists are at the core of developing the information required to address the concerns and to bridge the risk divide. In this session, various stakeholders will share their experiences on how they have worked to address the divide between perceived risk versus actual risk as they develop regulations, formulate policies, and conduct and report research findings. Speakers are drawn from local stakeholder groups (i.e., industry, regulators, academia, and non-governmental organizations) to provide a variety of perspectives. The session will feature a risk communication specialist, who will provide some insight into overcoming the challenges. The goal of the session is to stimulate discussion on the role of toxicologists in risk and science communication, the challenges and solutions to effective communication on controversial public health issues, and the difficulty related with developing policy decisions on a polarizing issue. While OGD provides a case study, the issues faced by the oil and natural gas industry can be transposed across settings where public health concerns are elevated from public opinion.

Introduction. Erica Bruce, Baylor University, Waco, TX.

Industry Perspective on the Challenges Related to Communicating Risks for Unconventional Oil and Gas Operations. Uni Blake, American Petroleum Institute, Washington, DC.

Unconventional Natural Gas and Oil Drilling and Public Health in the Marcellus Shale. Trevor Penning, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA.

Perspectives from the Texas Commission on Environmental Quality (TCEQ) Related to Risk Communication and Unconventional Oil and Gas Operations in Texas. Tiffany Bredfelt, Texas Commission on Environmental Quality, Austin, TX.

Perspectives from a Risk Communication Expert: Focus on Unconventional Oil and Gas Operations. Vincent Covello, Center for Risk Communication, New York, NY.

Communication of Scientific Findings and Risk Perception Associated with Unconventional Oil and Natural Gas Development. Elena Craft, Environmental Defense Fund, Austin, TX.

Historical Highlights Session

Radiation Toxicity: Historical Perspective on Epidemiological and Experimental Evidence Informing Standards

Tuesday, March 13, 1:30 PM to 4:15 PM

Chairperson(s): *Roger McClellan, Toxicology and Risk Analysis, Albuquerque, NM; and Philip Wexler, National Library of Medicine, Bethesda, MD.*

Primary Endorser:
Specialty Section Collaboration and Communication Group

Other Endorser(s):
Carcinogenesis Specialty Section
Regulatory and Safety Evaluation Specialty Section

The literature on the health effects of external radiation exposures and internally-deposited radionuclides, most of which was developed post-World War II, is extraordinarily voluminous and robust. This literature includes information on the sources of radiation and radionuclides, environmental and occupational exposures, substantial epidemiological findings, and complementary findings from controlled exposures of molecules, cells, tissues, and populations of multiple species of laboratory animals. The substantial scientific literature has been used to inform the settings of radiation exposure standards for workers and the general population. The radiation protection scheme takes account of radiation quality and dose protraction. The presentations in this session will briefly review the history of key discoveries in the radiation field and the development of radiation protection standards, as well as the historical development of knowledge on radiation effects discovered using both epidemiological and experimental approaches.

Mutations and cancer, which have traditionally been primary endpoints in radiation protection standards, will be highlighted. Various models describing radiation dose-response relationships, including the use of the linear no-threshold model, will be covered. Uncertainties and controversies in the knowledge base will be discussed, including the extent to which the setting of radiation protection standards has subsequently influenced the standard setting for chemical exposures. Further, in light of the thousands of nuclear weapons stockpiled around the world, this session also will put into perspective the human and environmental consequences of ionizing radiation that could ensue from their potential use.

Key Historical Events in the Discovery of Radiation Phenomena and Sources of Radiation Exposure. Philip Wexler, National Library of Medicine, Bethesda, MD.

History of Radiation Protection Standards. John Poston Sr., Texas A&M University, College Station, TX.

Key Epidemiological Findings on Health Effects of External Exposure and Internally-Deposited Radionuclides, with an Emphasis on Cancer as an Endpoint. David Hoel, The Medical University of South Carolina, Charleston, SC.

Role of Studies with Internally-Deposited Radionuclides in Laboratory Animals to Inform Radiation Protection Standards. Roger McClellan, Toxicology and Risk Analysis, Albuquerque, NM.

Role of Molecular and Cellular Data in Radiation Risk Assessment. Antone Brooks, Washington State University (Retired), Pullman, WA.

Early Efforts to Develop Quantitative Exposure-Cancer Response Models for Chemically-Induced Cancer. Kenny Crump, Louisiana Tech University, Ruston, LA.

Education-Career Development Session

Perfecting Your "Elevator Speech"

Tuesday, March 13, 4:30 PM to 5:50 PM

Chairperson(s): *Joseph Cichocki, Alnylam Pharmaceuticals, Cambridge, MA; and Kathryn Page, The Clorox Company, Pleasanton, CA.*

Primary Endorser:
Career Resource and Development Committee

Other Endorser(s):
Education Committee
Postdoctoral Assembly

Effectively communicating science to the general public and to experts in the field is a skill that must be mastered in order to build your career. For most individuals, and especially most trainees, orally presenting a seminar or formalized science speech is much easier than giving a brief, two-to-three minute talk about one's science and its impact on the general public. This "elevator speech," however, is often the most important talk one will ever give, as you often have to communicate your science in a brief, succinct, and clear fashion in order to convey your message to lay individuals and experts alike. Further, during job interviews, you will not have one hour to talk to every interviewer individually, but, rather, will have to quickly summarize your work in a couple of minutes. This session will provide tips and tricks to deliver your "elevator speech," which will be useful for your interactions not only at the SOT Annual Meeting and ToxExpo, but also in your daily professional (and maybe personal) life. Following a brief introduction, a panel of experts and early-career scientists will provide examples and advice on how to quickly summarize a scientific project into a brief two-to-three minute speech. Following the short panel discussion, a 35-minute "hands-on" session will follow in which the session chairs will facilitate attendees as they perform their two- to three-minute "elevator speeches" in small groups. Five minutes will be allocated to wrap-up the session following the hands-on activity.

Introduction. Joseph Cichocki, Alnylam Pharmaceuticals, College Station, TX.

Body Language and First Impressions. Marie Fortin, Alcami Corporation, Piscataway, NJ.

Perfecting Your Pitch: Key Features of an Elevator Speech to Help You Reach the Top Floor. Shaun McCullough, US EPA, Chapel Hill, NC.

What NOT to Do… Ruth Roberts, ApconiX, Alderley Edge, United Kingdom.

Panel Discussion/Q&A. Kathryn Page, The Clorox Company, Pleasanton, CA.

Hands-On Activity. Joseph Cichocki, Alnylam Pharmaceuticals, Cambridge, MA.

Workshop Sessions

Cardiovascular Adverse Effects Are Still Causing Late Attrition of Novel Therapeutics: Developing Solutions to Detect and Avoid Cardiovascular Toxicity in the Clinic

Wednesday, March 14, 8:00 AM to 10:45 AM

Chairperson(s): *John Kremer, Covance, Madison, WI; and Mark Holbrook, VAST Pharma Solutions, Harrogate, United Kingdom.*

Primary Endorser:
Cardiovascular Toxicology Specialty Section

Other Endorser(s):
Drug Discovery Toxicology Specialty Section
Regulatory and Safety Evaluation Specialty Section

Cardiovascular (CV) liabilities continue to be a leading cause of drug attrition in late-stage clinical trials and post-market approval. Aspects of the current paradigm have adequately characterized (e.g., benefit vs. risk) compounds for hERG blockade and QT interval prolongation, but a method to detect arrhythmogenesis directly, rather than using surrogates, still needs to be defined. Even so, the rate of attrition due to CV liabilities has remained intractably high, primarily due to non-QTc-related liabilities (e.g., blood pressure, contractility). This session will start by highlighting several high-profile drug withdrawals due to unexpected CV liability to establish the problem statement. Specific examples will include Terfenidine (QT prolongation, Torsades de Pointes); Vioxx/COX-2 inhibitors (myocardial infarction, stroke); and Torcetrapib (increased cardiac events, hypertension). The individual speakers will address this problem by describing new scientific and strategic approaches to detect and characterize potential liabilities, culminating in a panel discussion with the audience. Specifically, the first presentation will describe the use of human-induced pluripotent stem cell-derived cardiomyocytes to profile safety and potential mechanisms for drug-induced arrhythmia or structural cardiotoxicity. The second and third presentations will focus on the use of rodent and large animal models, respectively, in safety (normal healthy animals) or efficacy (disease models) studies, including key considerations, such as study design, model selection and characterization, and translatability to clinical endpoints. The fourth presenter will add to the discussion of translation from preclinical (*in vitro*, *ex vivo*, *in silico*, and *in vivo*) to clinical and the importance of statistical power to delineate a positive vs. negative signal for a better integrated CV risk assessment. The final presenter will build on this discussion of statistical sensitivity by presenting a retrospective analysis of power for CV data reported in recent investigational new drug (IND) submissions and a regulatory viewpoint on the use of alternative *in vivo* models. The session will end with a brief summary of strategies to improve CV safety assessment to enhance patient safety and reduce the risk of compound failure and will be followed by a panel discussion to outline how researchers across multiple disciplines and organizations can share approaches and data to improve the testing paradigm. The goal of the session is to provide a data-driven, comprehensive discussion on how to revise CV safety assessments to improve patient safety and reduce the rate of late-stage compound failures.

Introduction. John Kremer, Covance, Madison, WI.

Use of hiPSC-Derived Cardiomyocytes for Cardiac Safety Evaluation. Liang Guo, Frederick National Laboratory for Cancer Research, Frederick, MD.

Incorporation of Cardiovascular Assessment in Early Efficacy or Safety Studies in Rodents. Richard Macia, Covance, Madison, WI.

Clinically-Relevant Large Animal Models of Heart Failure: Model Selection, Limitations, and Optimization. Kim Hoagland, Amgen, Thousand Oaks, CA.

Translation from Nonclinical to Clinical Cardiovascular Safety: What Constitutes a Safety Risk? Mark Holbrook, VAST Pharma Solutions, Harrogate, United Kingdom.

A Regulatory Discussion of Cardiovascular Safety Pharmacology Studies. Donald Jensen, US FDA, Washington, DC.

Environmental Chemical-Microbiome Interactions in Disease Susceptibility

Wednesday, March 14, 8:00 AM to 10:45 AM

Chairperson(s): *Mitzi Nagarkatti, University of South Carolina, Columbia, SC; and Gary Perdew, Pennsylvania State University, University Park, PA.*

Primary Endorser:
Comparative and Veterinary Specialty Section

Other Endorser(s):
Biotechnology Specialty Section
Toxicologic and Exploratory Pathology Specialty Section

The human body harbors trillions of microbes, and there exists a symbiotic association between humans and microbes. Such an interaction plays a critical role in maintaining homeostasis. Because the microbial ecosystem is found throughout the body, it is constantly exposed to environmental chemicals. Thus, there is constant crosstalk between the environmental chemicals and microbiota, leading to altered bioavailability of chemicals and/or microbial dysbiosis that could trigger disease process. To that end, it is critical to get a better understanding of the mechanisms of these complex interactions between environmental chemicals and microbiota. Such studies may help in understanding why certain individuals are more susceptible to certain diseases when compared to others. This session will explore recent findings that provide conclusive answers, demonstrating that certain environmental insults cause microbial dysbiosis and consequently trigger various diseases. This session will start with introduction to the field, followed by a presentation of data on how bacterially-generated and exogenous chemicals alter the bacterial composition and metabolism within the gut, leading to altered host homeostasis by activating the Ah receptor (AhR). The session will provide evidence that inhalation of Staphylococcal enterotoxin-B (SEB) triggers acute lung injury (ALI) in mice that can be effectively blocked by resveratrol, an AhR ligand. Interestingly, SEB triggered dysbiosis in the lung and gut microbiota, thereby suggesting gut-lung axis. Moreover, resveratrol treatment reversed the dysbiosis, thereby suggesting that AhR activation may prevent SEB-induced inflammation through alterations in the microbiome. Presenters will provide evidence that specific microbial genotoxic activities originating from various microbial strains, such as *Escherichia coli, Atopobium parvulum,* and *Campylobacter jejuni,* promote development of colorectal cancer (CRC). Also, it will be demonstrated that CRC development could be modulated using genetic and pharmacological intervention aimed at the

microbiota. These studies represent the first step toward validating the microbiota as a potential therapeutic target for prevention/treatment of CRC. Presenters will discuss obesogenic chemicals and describe how they interact with gut microbiota and promote adiposity in animals. Talks will focus on obesogenic activity of tributyltin. Together, the presentations will be organized in such a way that they will transition from introducing the topic on how crosstalk between environmental chemicals and microbiota plays a critical role in health and disease to addressing, in the second talk, more specific questions, such as the gut-lung axis in regulating the inflammatory disease. The third and fourth presenters will focus on specific disorders, such as cancer and obesity, with the third talk also highlighting how altering the microbiota would serve as a therapeutic tool to prevent/treat colon cancer. Together, this workshop will provide an exciting opportunity for all participants to gain new knowledge of the complexity of the interactions between the environmental chemicals to which people are constantly exposed and the microbiota, as well as novel insights into how they regulate the pathogenesis of a variety of clinical disorders.

Modulation of the AhR within the Gastrointestinal Tract Mediates Both Protective and Adverse Outcomes. Gary Perdew, Pennsylvania State University, University Park, PA.

Staphylococcus Enterotoxin B (SEB) Triggers Acute Lung Injury (ALI) through Dysbiosis in Gut-Lung Axis and AhR Ligands Protect the Lungs through Reversal of Microbiome. Mitzi Nagarkatti, University of South Carolina, Columbia, SC.

Tributyltin Exposure Alters Post-Embryonic Growth, Adiposity, and Intestinal Microbiota Assembly in Zebrafish. John Rawls, Duke University School of Medicine, Durham, NC.

Cancer: Mining the Microbiota for Answers. Christian Jobin, University of Florida, Gainesville, FL.

IAT Matching Analytical Methods to Markets: Balancing Regulatory Expectations and Technical Challenges

Wednesday, March 14, 8:00 AM to 10:45 AM

Chairperson(s): *Barbara Henry, W.L. Gore & Associates, Inc., Elkton, MD; and Sherry Parker, WuXi AppTec, St. Paul, MN.*

Primary Endorser:
Medical Device and Combination Product Specialty Section

Today, regulators, supply chain partners, and customers want to know what is in the products they buy that might harm them. From a risk assessment perspective, the absence of clear consensus and regulatory guidance for chemical characterization of medical devices, drug-device combination products, and their components delays commercialization of life-benefiting technology, leads to increased animal testing as a clearly-defined path to market, and is expensive. This session will seek to open the dialogue on the challenges and potential paths forward for manufacturers of medical devices, device-drug combination products, and manufacturers of components to those industries. The first presenter will briefly compare several extractables and leachables (E&L) approaches, including ISO 10993 and those by the United States Pharmacopeia, Product Quality Research Institute, the US Food and Drug Administration (US FDA), the Extractables Work Group of the BioPhorum Operations Group, and the Bio-Process Systems Alliance. Once the stage is set, the next presenter will focus on ISO 10993 -1, -17, and -18 acknowledging the importance of chemical characterization of medical devices, as well as the current lack of sufficient detail to plan extraction, analysis, and interpretation for risk assessment. Proposed revisions to the standards and guidance will be discussed. Remember the expression "garbage in, garbage out"? In order to have high-quality risk assessments, the data must be high quality. The next topic will be the essential collaboration between the chemist and toxicologist in the design, execution, and interpretation of E&L studies. Knowing what the product is made with, manufacturing steps, potential contaminants, residuals, and impurities helps the toxicologist identify potential chemicals of concern, which the chemist will then need to find and quantify using appropriate solvents, extraction conditions, and analytical techniques. How low should you go (limit of detection) to support the risk assessment for the intended use of the product? When to be aggressive in extractions and when to use "kinder and gentler" extractions simulating clinical-use conditions of products will be addressed. This topic will end with risk assessment approaches, including handling of unknown chemicals and use of the Threshold of Toxicological Concern (TTC) for a permanently-implanted medical device and a drug-device combination product. Now, that the opening presentations have shared a collaborative plan of attack for E&L, does it matter which lab does the analysis? Inter-laboratory variability related to compound identification and quantitation, including equipment sensitivity and the available chemical library, will be discussed by the next presenter. Disparity in the number of reported compounds among four test laboratories for the same test articles, despite the same extraction solvents, conditions, and analytical techniques, will be shared. Considerable quantitative and qualitative differences potentially impacting the risk assessment will be discussed. The final presentation will provide light at the end of this complex and complicated tunnel by sharing US FDA expectations of E&L studies for medical devices and combination products. The presentation will include LODs, LOQs, sensitivity, extraction methods, and the interpretation of qualitative, semi-quantitative, and quantitative data, as well as issues frequently encountered. To close out the session, the panel will answer audience questions regarding lab selection, unknowns, use of the TTC, Cramer Classes, and *in silico* approaches. This session will feature information and provocative discussions that will be transferable to other E&L applications and should be of interest to contract labs and manufacturers of parts intended for use in medical devices, pharmaceutical processing, or single-use systems, as well as regulators.

Introduction. Barbary Henry, W.L. Gore & Associates, Inc., Elkton, MD.

Which Guidance to Follow for Which Market? Barbara Henry, W.L. Gore & Associates, Inc., Elkton, MD.

Extractables and Leachables Testing for Medical Devices—What About ISO 10993 Series? Albrecht Poth, Dr. Knoell Consult GmbH, Mannheim, Germany.

Designing Chemical Characterization Studies for Medical Devices and Combination Products with the Risk Assessment in Mind: Current Approaches and Challenges. Sandi Schaible, WuXi AppTec, St. Paul, MN.

Variation in Chemical-Characterization Results from Four Test Laboratories. Monica Posgai, Johnson & Johnson, Cincinnati, OH.

An Overview of Regulatory Considerations for Chemical Characterization of Medical Devices and Combination Products. Ji Guo, US FDA Center for Devices and Radiological Health, Silver Spring, MD.

Q&A—Seed Questions and Audience Participation. Sherry Parker, WuXi AppTec, St. Paul, MN.

IAT Mechanisms of Ocular Sulfur Mustard Toxicity and Potential Therapies

Wednesday, March 14, 8:00 AM to 10:45 AM

Chairperson(s): *Vasilis Vasiliou, Yale School of Public Health, New Haven, CT; and Marion Gordon, Rutgers, The State University of New Jersey, Piscataway, NJ.*

Primary Endorser:
Ocular Toxicology Specialty Section

Other Endorser(s):
Women in Toxicology Special Interest Group

Sulfur mustard is a chemical weapon used in World War I and the Iran-Iraq War of the 1980s. The US government still lists it as a potential warfare and terrorist agent. While exposures are often not lethal, long-term or recurrent damage to the eyes, skin, and lungs can occur. Sulfur mustard is presently a concern because it has been reported that ISIS has produced and used sulfur mustard against its adversaries. In an ISIS conflict with Syrians on August 21, 2015, unsuspecting victims developed blisters, and sulfur mustard residue was confirmed on pieces of artillery shells. Individuals do not usually feel exposure to sulfur mustard exposure until a few hours after it has occurred. This results in confusion and panic, making mustard an ideal terrorist agent. To date, there are no US Food and Drug Administration-approved therapies to treat sulfur mustard exposure of any organ, partly due to the fact that the mechanisms of toxicity of mustards are not yet well-understood. Because of government restrictions on the use of sulfur mustard, academics often use nitrogen mustard for preliminary exposures experiments and subsequently confirm their results with sulfur mustard exposures performed by companies or the Department of Defense, who are authorized to use the agent. The goal of this session is to highlight: 1) research resulting in new information on molecular pathways activated by mustard exposure; 2) new developments in how ocular exposures are performed to attain the most reliable and reproducible injury; and 3) research efforts using the newer molecular pathway information to identify potential therapies for ocular sulfur mustard exposure. Speakers will include an industry representative providing a new method of ocular mustard exposure, as well as researchers from academic, federal, and private institutions who are using the recently-identified mechanisms of mustard toxicity to identify potential ocular therapies.

Introduction. Vasilis Vasiliou, Yale School of Public Health, New Haven, CT.

CounterACT: Countermeasures against Chemical Threats—Ocular Exposures. Houmam Araj, NIH National Eye Institute (NEI), Bethesda, MD.

Acute and Chronic Pathologies in the Corneal Endothelium Following Ocular Sulfur Mustard Exposure: A New Model of Corneal Injury Progression. Patrick McNutt, US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD.

Ocular Injuries by Vesicating Agents: Models and Development of Medical Countermeasures. Neera Tewari-Singh, University of Colorado, Aurora, CO.

Engineered FGF-1s as Therapeutics for Ocular Vesicant Injury. David Eveleth, Trefoil Therapeutics, LLC, San Diego, CA.

Reaching Hazard Conclusions for Endocrine-Disrupting Chemicals: Adapting Systematic Review Methods

Wednesday, March 14, 8:00 AM to 10:45 AM

Chairperson(s): *Johanna Rochester, The Endocrine Disruptor Exchange (TEDX), Grand Junction, CO; and Vickie Walker, NIEHS, Research Triangle Park, NC.*

Primary Endorser:
Reproductive and Developmental Toxicology Specialty Section

Other Endorser(s):
Neurotoxicology Specialty Section
Risk Assessment Specialty Section

Reviews of environmental chemicals, such as endocrine-disrupting chemicals (EDCs), are essential for identifying hazards to the health of humans and wildlife, yet they often lead to inconclusive results that can stall the regulatory process. Attempts to review this literature to arrive at hazard conclusions are often unstandardized, including weight of evidence reports or narrative reviews that lack transparency and reproducibility. To address this, systematic review methods have been developed to evaluate environmental health questions. These methods include the Office of Health and Translation (OHAT) Approach for Systematic Review, the University of California San Francisco (UCSF) Navigation Guide, and the systematic review and integrated assessment (SYRINA) of EDCs. Systematic review methodology increases the objectivity and transparency in an evaluation by using a pre-defined, multistep process to identify, critically assess, and synthesize evidence. They also contain specific methods to address study quality, among other factors. When appropriate, systematic reviews employ meta-analytical techniques that can help in the interpretation of apparently conflicting results and provide a clearer picture summarizing the overall body of evidence. These methodologies are adapted from the medical field, which has developed, used, and empirically tested systematic review methods to evaluate medical research and reach evidence-based clinical decisions about patient care and interventions. Recognition of the value of systematic review methods has increased among the environmental health community over the last five years. In fact, the US National Academy of Sciences (NAS) recently convened a panel to evaluate how systematic review procedures can be used as part of an overall strategy to evaluate potential "low-dose" endocrine-mediated effects for environmental chemicals. The NAS panel, consisting of experts from academia, non-government organizations, government, and industry, developed systematic reviews of two EDCs to illustrate the utility of systematic reviews in decision making. The resulting report will use the systematic reviews to conclude if the data support a likely causal association, evaluate the nature and relevance of dose-response relationships, and discuss how human and animal data streams can be integrated. This session will outline systematic review approaches in environmental health from government, academic, and industry perspectives. It will begin with an overview of systematic review methods in environmental health, including the SYRINA systematic review framework developed specifically for EDCs, which provides a method to identify chemicals as EDCs and assesses the strength of the association between exposure and adverse outcome. The next talk will present a case study using the UCSF Navigation Guide approach to investigate the neurotoxic effects of polybrominated diphenyl ethers (PBDEs), as an example of non-reproductive health

effects associated with EDCs. The last two speakers are members of the NAS committee and will provide an overview of the timely, cutting-edge evidence and insight from the NAS panel's report of systematic review use in low-dose environmental toxicology, including its role in regulatory toxicity practices. The NAS strategy and recommendations for evaluating low-dose adverse effects that act through endocrine-mediated pathway will be outlined. The NAS report developed case studies that examined low-dose adverse effects of two EDCs: PDBEs and phthalates. These case studies will be used to illustrate how systematic review methods can be used to evaluate human and animal evidence of adverse effects of EDCs, considerations for health effects evidence and dose-response concordance in integrating the human and animal evidence, and how a published systematic review can be critically evaluated and used when the focus is appropriate for the research question under consideration. They also will discuss the committee's recommendations for moving forward in integrating systematic review methods for evidence-based decision and policymaking.

Introduction: Systematic Review and Environmental Health. Johanna Rochester, The Endocrine Disruption Exchange (TEDX), Grand Junction, CO.

SYRINA: Developing a Method for the Systematic Review of EDC Studies. Laura Vandenberg, University of Massachusetts Amherst, Amherst, MA.

PDBEs and Neurodevelopment: A Systematic Review Using the Navigation Guide. Juleen Lam, University of California San Francisco, San Francisco, CA.

NAS Case Study on Developmental Reproductive Effects. Andrew Rooney, NIEHS, Research Triangle Park, NC.

Phthalate Male Reproductive Toxicity: Comparison of Hazard Conclusions and Dose Responses from the NAS Systematic Review and Traditional Toxicity Testing Studies. Kamin Johnson, The Dow Chemical Company, Midland, MI.

Reducing the Uncertainty of Read-Across Predictions by New Approach Methodologies: Application in Regulatory Human Risk Assessments

Wednesday, March 14, 8:00 AM to 10:45 AM

Chairperson(s): *Ivan Rusyn, Texas A&M University, College Station, TX; and Nicole Kleinstreuer, NTP NICEATM, Durham, NC.*

Primary Endorser:
Regulatory and Safety Evaluation Specialty Section

Other Endorser(s):
***In Vitro* and Alternative Methods Specialty Section**
Risk Assessment Specialty Section

A paradigm shift is ongoing in human risk assessment, away from the traditional *in vivo* animal studies towards new approach methodologies (NAM). NAM include *in vitro*, *ex vivo*, or 'omic technologies, as well as *in silico* and toxicokinetic modeling. Currently, hazard assessment and derivation of point of departure values are based on the apical toxicity findings in animal studies. These apical endpoints seldom provide detailed mechanistic information to inform extrapolation of these findings to humans. NAM have the potential to provide a deeper understanding of key and intermediate steps leading to a certain apical finding, a concept known as adverse outcome pathways (AOP). However, the integration of NAM data into risk assessments is challenging, in particular for complex endpoints, such as repeated dose or reproductive toxicity. This session will provide an in-depth overview of the use of NAM in regulatory and investigative toxicology, starting with a regulatory perspective, followed by industry examples, and then broadening the scope to cover the most up-to-date developments from the EU-ToxRisk and US academic and government research programs. A focus will be on read-across case studies, by which the use of NAM and mechanistic data is demonstrated. Learnings from the proof-of-concept read-across approaches and case examples will help to develop new mechanism-based chemical safety testing strategies. This session will include a discussion on the limitations and advances of such approaches and the path forward to substantiate and support a paradigm shift in regulatory risk assessment practices.

Use of Read-Across under the REACH Regulation. Mike Rasenberg, European Chemicals Agency (ECHA), Helsinki, Finland.

How Can Read-Across Be Substantiated with Additional Biological Data? Learnings from Industry Submissions. Hennicke Kamp, BASF, Ludwigshafen am Rhein, Germany.

EU-ToxRisk Case Studies: New Approach Methodologies in Read-Across. Sylvia Esccher, Fraunhofer ITEM, Hanover, Germany.

Categorization of UVCBs Using Chemical-Biological Read-Across. Ivan Rusyn, Texas A&M University, College Station, TX.

Current and Future Opportunities for US Regulatory Application of Read-Across. Nicole Kleinstreuer, NTP NICEATM, Durham, NC.

Roundtable Sessions

Is a Common Mechanism of Action Essential to Conduct a Cumulative Risk Assessment or Just Nice to Have?

Wednesday, March 14, 11:00 AM to 12:20 PM

Chairperson(s): *Suzanne Fitzpatrick, US FDA, College Park, MD; and Elaine Faustman, University of Washington, Seattle, WA.*

Primary Endorser:
Mixtures Specialty Section

Other Endorser(s):
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

Current risk assessments of chemicals for regulatory purposes do not generally take into account the "real-life" exposure to multiple substances, but rely instead on the assessment of individual substances in individual commodities. Humans, however, are routinely exposed simultaneously to numerous chemicals via multiples routes of exposure. These mixtures can be variable, constantly changing, and essentially undefinable. One major question is whether a common mechanism of action is a critical element for conducting a cumulative risk assessment. The complex toxicology of chemical mixtures and the diversity of the routes of exposure may call for the development of both mechanism-based and non-mechanism-based quantitative frameworks for risk assessment to estimate the impact on health, thereby increasing the efficiency and effectiveness of these evaluations. Consideration of the new testing concepts, such as *in vitro* models, the exposome, adverse outcome pathways, and computational models, and how this may help inform our discussion on chemical mixtures will be included in the roundtable talks. This roundtable will conclude with a debate on the different approaches to assess the potential health impacts of exposure to chemical mixtures.

Why the Confusion on Mixture Risk Assessment? Elaine Faustman, University of Washington, Seattle, WA.

The US EPA Approach to Evaluating Mixtures. Evisabel Raig, US EPA, Washington, DC.

Risk of Mixtures Should Be Assessed on a Case-by-Case Basis Depending on the Available Data. A. Wallace Hayes, Harvard T.H. Chan School of Public Health, Boston, MA.

The EuroMix Project: Defining International Strategies for Mixtures Risk Assessment. Alan Boobis, Imperial College London, London, United Kingdom.

Panel Debate: State of the Science, or What to Advise Scientists on How to Conduct a Mixtures Risk Assessment. Suzanne Fitzpatrick, US FDA, College Park, MD.

Unlocking the 'Omics Archive: Enabling Toxicogenomic/Proteomic Investigation from Archival Samples

Wednesday, March 14, 11:00 AM to 12:20 PM

Chairperson(s): *Deidre Dalmas, GlaxoSmithKline, King of Prussia, PA; and Susan Hester, US EPA, Research Triangle Park, NC.*

Primary Endorser:
Clinical and Translational Toxicology Specialty Section

Other Endorser(s):
Molecular and Systems Biology Specialty Section
Toxicologic and Exploratory Pathology Specialty Section

Formalin fixation and paraffin embedding (FFPE) is a cross-industry gold standard for preparing nonclinical and clinical samples for histopathological assessment which preserves tissue architecture and enables storage of tissue in archival banks. These archival banks are an untapped resource and vast repository of tissue from regulatory toxicology studies, novel animal bioassays, clinical trials, or epidemiologic studies with corresponding detailed pathological assessments. Although these FFPE archives hold keys to various unknown mechanisms and/or disease processes, direct use of archival samples for transcriptomic or proteomic profiling has been relatively limited. Formalin fixation degrades RNA and results in cross-linking and fragmentation, which is thought to significantly impair transcriptomic/proteomic analyses. Because of the roadblocks, there is a need to develop novel methods that can reliably access gene and protein information from FFPE tissue-enabling retrospective investigations from pathologically-anchored samples, which would otherwise be very costly and require additional patient or animal samples to retest in order to obtain this information from prospectively-collected frozen tissue. The goal of this session is to highlight recently-developed novel approaches to reliably access quantitative gene and protein information from FFPE tissue and convey how these approaches can be used to interrogate mechanisms of toxicity and aid in biomarker development/analysis from both nonclinical and clinical samples. The session will first showcase novel methods to overcome limitations of using FFPE tissue archived for four and a half years, enabling access to robust transcriptomic and proteomic information from nonclinical regulatory toxicology studies, and how these approaches have been utilized to support regulatory filings. The session will then highlight and compare gene expression profiles derived from archived FFPE tissue preserved in formalin for eight, 19, and 26 years, using novel methods developed for DNA microarray analysis, as well as exosome enrichment approaches utilizing nucleic acid samples and whole-transcriptome sequencing (RNA-Seq) library preparation methodologies. Despite individual efforts across the industry, methods to enable RNA-Seq evaluation from limiting quantities and quality RNA was, until recently, still not possible. Because the issue is too complex to be solved by individual organizations working in isolation and with limited resources, the ILSI Health Environmental and Sciences Institute (HESI) Genomics Committee FFPE Working Group has been developing methods to "demodify" FFPE RNA, enabling subsequent, more robust RNA-Seq analysis. Novel methods developed to improve RNA yield and sequencing results from limiting quantities and quality RNA FFPE samples will be highlighted, followed by a comparison across frozen and FFPE samples fixed under varying alcohol and/or formalin conditions. Lastly, development and utilization of novel methods to enable global proteomic and phosphoproteomic analysis

of case matched frozen and FFPE clinically-derived samples using mass spec-based technologies will be emphasized. Utilization of the novel methods described, now enable retrospective generation of quantitative gene and protein information from phenotypically-anchored archival nonclinical and clinical FFPE tissue to interrogate mechanisms of toxicity, aid in biomarker development, enable creation of a critical translational bridge between emerging *in vitro* and *in vivo* data, and evaluation of chemically-induced adverse health effects established in prior toxicologic and epidemiologic studies, as well as enabling data gaps to be closed in adverse outcome pathways (AOPs).

Introduction. Raegan O'Lone, ILSI Health and Environmental Sciences Institute (HESI), Washington, DC.

Understanding Benefits and Limitations of Formalin-Fixed Paraffin-Embedded (FFPE) Tissue Enables Retrospective Nonclinical Genomic and Proteomic Investigations. Deidre Dalmas, GlaxoSmithKline, King of Prussia, PA.

Finding Salvation in Degradation—Using Degraded Formalin-Fixed Paraffin-Embedded (FFPE) Samples for RNA Sequencing. Christopher Mason, Weill Cornell Medical College, New York, NY.

Demodification Methods for Improving Quality of RNA from Formalin-Fixed Paraffin-Embedded (FFPE) Samples (ILSI HESI Genomics Committee). Susan Hester, US EPA, Research Triangle Park, NC.

Global Proteomic and Phosphoproteomic LC-MS Analysis of Case Matched Frozen and Formalin-Fixed Paraffin-Embedded (FFPE) Tissues. Daniel Chelsky, Caprion Biosciences, San Francisco, CA.

Informational Session

Good Cell and *In Vitro* Method Practices against the "Reproducibility Crisis"

Wednesday, March 14, 11:00 AM to 12:20 PM

Chairperson(s): *David Pamies, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; and Sandra Coecke, European Commission Joint Research Centre, Ispra, Italy.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

Other Endorser(s):
Stem Cells Specialty Section

There is a strong belief that *in vitro* methods are fast becoming the key tool for a new way of doing toxicology. However, their potential will not be fully realized if they are not developed and applied in a way in which scientific integrity and quality are assured—the data they produce will not be trusted by decision makers. A revealing paper (*Nature* 2016, 533:452–454) showed that 70% of researchers have tried and failed to reproduce another scientist's experiment, and more than half of the researchers failed to reproduce their own experiments. These dramatic data call for incentives for better practice. With the development of new high-throughput technologies, stem cells, and new culture technologies (organo-typical cell cultures, organ-on-a-chip technologies), new challenges are presented for reproducibility of such advanced test systems. This session will summarize the challenges of working with *in vitro* cell and tissue-based culture methods and will describe the different initiatives that have taken place in recent years to give guidance on good cell and good *in vitro* method practices as measures against the reproducibility crisis in science. The session also will elaborate on the use of human-induced pluripotent stem cell-based systems for regulatory purposes and how to validate the new generation of high-throughput *in vitro* methods and microphysiological systems.

21st-Century Cell Culture for 21st-Century Toxicology. David Pamies, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

Development of an OECD Guidance Document on Good *In Vitro* Method Practices (GIVIMP). Sandra Coecke, European Commission Joint Research Centre, Ispra, Italy.

Good Cell Culture Practice in the Development of Human Pluripotent Stem Cell-Based Systems. Glyn Stacey, Institute of Biomedical Science, London, United Kingdom.

Validation of *In Vitro* Cell-Based Assays for the Tox21 Program. Menghang Xia, NIH, Bethesda, MD.

Systematic Characterization of Microphysiological Systems (MPS). Murat Cirit, Massachusetts Institute of Technology Genomics Facilities Core, Rock Point, VA.

Education-Career Development Session

Career Opportunities in Regulatory Toxicology

Wednesday, March 14, 11:00 AM to 12:20 PM

Chairperson(s): *William Farland, Colorado State University and William H. Farland Consulting, LLC, Rockport, ME; and Angela Lynch, ToxPlus Consulting and Roosevelt University College of Pharmacy, Haymarket, VA.*

Primary Endorser:
Education Committee

Other Endorser(s):
Regulatory and Safety Evaluation Specialty Section
Risk Assessment Specialty Section

This session will serve as an introduction to current issues and opportunities in regulatory toxicology for graduate students and early-career scientists, as well as to motivate them to seek training experiences that will increase their knowledge of the approaches to and challenges of bringing modern-day toxicology into a risk or safety assessment process. The SOT Graduate Education Subcommittee, via its Awareness of Regulatory Toxicology (ART) Working Group, has assembled experts in regulatory toxicology to discuss opportunities available for toxicology trainees and others interested in pursuing careers in regulatory toxicology. Resources developed by ART for trainees interested in these careers also will be presented to attendees. Regulatory bodies within the United States and other countries use scientific data from various sources to assess the safety of chemicals and drug candidates in order to inform regulatory policy and determine approvals for use. In turn, industry uses scientific data to meet regulatory requirements and to achieve product stewardship and sustainability goals.

Training in and application of modern, laboratory-based science must be married to the legislative and regulatory processes in order to inform decisions that are understandable and benefit the public. Many toxicology and postdoctoral training programs do not cover regulatory toxicology or regulatory processes to a significant degree. In addition, scientists who engage in the regulatory process through advisory boards or public comment on specific issues may not be fully aware of the regulatory process and/or impacts of regulatory decisions. Although toxicologists often gain experience while on the job, accessing training or internships in regulatory toxicology early in a scientist's career benefits trainees by increasing knowledge of how scientific data can be used in the public domain, as well as by increasing awareness of available job opportunities. In addition, knowledge of the regulatory use of toxicology information also benefits toxicologists considering service in an advisory capacity to government or industry.

Introduction. Angela Lynch, ToxPlus Consulting and Roosevelt University College of Pharmacy, Haymarket, VA.

Training in Regulatory Toxicology: Understanding Opportunities and Present-Day Challenges. James Klaunig, Indiana University, Bloomington, IN.

The Role of Regulatory Toxicology in Drug Development. Tao Wang, Achaogen, San Francisco, CA.

Generating Toxicology Data to Meet the Needs of Regulatory Agencies. Allison Greminger, ExxonMobil Biomedical Sciences, Inc., New York, NY.

Evolving Approaches in Regulatory Toxicology: Integrating Pathway-Based Screening and Testing to Support Modern Chemical Safety Assessments and Harmonize International Approaches. David Dix, US EPA, Washington, DC.

Panel Discussion/Q&A. William Farland, Colorado State University and William H. Farland Consulting, LLC, Rockport, ME.

Symposium Sessions

Atherosclerosis as a Model to Understand the Combined Effects of Environmental Chemical and Non-Chemical Stressors

Wednesday, March 14, 1:30 PM to 4:15 PM

Chairperson(s): *Danielle Carlin, NIEHS, Research Triangle Park, NC; and Michelle Olive, NHLBI, Bethesda, MD.*

Primary Endorser:
Mixtures Specialty Section

Other Endorser(s):
Cardiovascular Toxicology Specialty Section
Molecular and Systems Biology Specialty Section

Atherosclerosis can lead to cardiac infarction and stroke and is a foremost candidate for identifying health effects associated with chemical and non-chemical stressors since much is known about the morbidity and mortality of this multifactorial disease. However, the evaluation of cumulative human health effects from multiple environmental exposures (i.e., chemical and non-chemical) represents a special research challenge due to the inherent complexity of the topic and requires careful examination of the potential interaction of these exposures. For example, further exploration is required of the biological mechanisms/pathways by which exposure to both environmental chemicals (e.g., air pollution, polycyclic aromatic hydrocarbons, metals, polychlorinated biphenyls, pesticides, and endocrine-disrupting chemicals) and non-chemical stressors (e.g., psychosocial, lifestyle, quality-of-life, poor nutrition, and physical stressors) over time leads to health effects and the roles the stressors may play in the development of diseases known to be associated with them (e.g., cancer, cardiac, metabolic, neurological, etc.). For the purposes of this session, combined exposures pertain to any set of environmental chemicals and non-chemical stressors that may contribute jointly to adverse human health outcomes, irrespective of whether people are exposed to the chemical(s)/non-chemical stressors at the same/different times or through similar/distinct sources or routes. Some of the other areas requiring further research on this complex topic include a better understanding of both the composition of real-world exposure to chemical and non-chemical stressors; the potential biological interactions between chemical and non-chemical stressors; and the development and validation of predictive models of combined exposure toxicity to characterize the hazard associated with these combined exposures. This session will bring together experts to discuss the state-of-the-science pertaining to underlying complex biological mechanisms/pathways associated with, when combined, chemical and non-chemical stressors in relation to atherosclerosis. Specifically, presentations will include a general overview of the etiology of atherosclerosis from chemical and non-chemical stressors, the biological mechanisms being evaluated by the extramural community, atherogenic mechanisms of environmentally-relevant chemicals, how diet and physical activity may modify atherosclerotic events, and how conceptual models can be created to evaluate complex causal pathways in this disease. In addition, this symposium also may be able to be used as a model for other diseases known to be associated with both chemical and non-chemical stressors and the roles these stressors may play in cumulative risk.

General Overview of the Public Health Burden of Atherosclerosis. Wayne Cascio, US EPA, Research Triangle Park, NC.

Non-Chemical Stressors in Atherosclerosis Research: The Extramural Portfolio Supported by the National Heart, Lung, and Blood Institute. Michelle Olive, NHLBI, Bethesda, MD.

Atherogenic Mechanisms of Superfund Chemicals. Sanjay Srivastava, University of Louisville, Louisville, KY.

Diet and Physical Activity as Modifiers of Pollutant-Induced Inflammatory Diseases: Implications in Atherosclerosis. Bernhard Hennig, University of Kentucky, Lexington, KY.

Using Conceptual Models to Evaluate the Complex Causal Pathways Involved in Cumulative Risk Assessment of Cardiovascular Disease. Charles Menzie, Exponent, Alexandria, VA.

Mechanisms of Autophagic Function and Dysfunction in Neurotoxicity and Neurodegeneration

Wednesday, March 14, 1:30 PM to 4:15 PM

Chairperson(s): *Johnny Wise, Purdue University, West Lafayette, IN; and Aaron Bowman, Vanderbilt University Medical Center, Nashville, TN.*

Primary Endorser:
Neurotoxicology Specialty Section

Other Endorser(s):
Graduate Student Leadership Committee
Metals Specialty Section

This session will be composed of graduate and postdoctoral trainees presenting primary research focused on autophagic pathways that go awry in neurodegenerative diseases and how relevant environmental toxicants affect these pathways. Autophagy is a tightly regulated catabolic process that enables a cell to conduct bulk degradation of protein aggregates or dysfunctional organelles in a specific or nonspecific manner. Autophagic pathways have been observed to be impaired under a variety of neurotoxic and neurodegenerative disease conditions. Further, environmental toxicants, such as neurotoxic metals, that are associated with altered risk or modification of neurodegenerative disease pathogenesis may interact with genetic risk factors of these diseases by disrupting autophagy. Investigation of these pathways is likely to provide key insight into early cellular events of these diseases, as disruptions to autophagic pathways occur prior to neurodegeneration or behavioral phenotypes. The session will begin with brief introductions regarding the structure of this trainee-led session and the trainees speaking, as well as a brief primer on autophagy and its potential role in neurodegenerative disease. In each talk, the trainee speakers will relate how autophagic dysfunction in their models contributes to disease pathogenesis and how their chemical(s) of interest exacerbate or ameliorate dysfunction. The first trainee speaker will discuss the role of autophagy in the toxicity of arsenic in cortical astrocytes. This speaker will present her findings on how AMPK and mTOR signaling regulate ATG5-dependent autophagy and apoptosis in astrocytes. The second trainee speaker will discuss the effects of manganese (Mn) exposure on autophagy-lysosome pathway in primary astrocytes, the mechanism(s) underlying Mn-induced autophagic dysregulation, and the functional relation between compromised autophagy and mitochondrial dysfunction. The third trainee speaker will continue the discussion

about Mn in Huntington's disease (HD), focusing on the contribution of excess manganese to neurons in HD and how the drug KB-R7943 can normalize Mn uptake. The fourth trainee speaker will change the topic to Parkinson's disease (PD) and will delve into how optineurin, a protein previously not considered in PD, contributes to pathogenesis through autophagic dysfunction. This speaker will emphasize the role of autophagic dysfunction on early mechanisms of PD and how they contribute to disease progression. The fifth trainee speaker will discuss the contribution of endosulfan to PD pathogenesis, as well as the relationship between autophagy and apoptosis in PD. The final trainee speaker will discuss the effects of low-dose chemical exposures on autophagic mechanisms in PD and further examine how these effects are altered even after chemical exposure is removed. Given that autophagy dysfunction is increasingly recognized as a common, early event in sporadic neurodegenerative diseases, it is imperative to understand how environmental chemicals disrupt normal autophagy pathways to gain a better understanding of disease pathogenesis, progression, and possible therapeutic intervention. Finally, the session will highlight the research program of six trainee SOT members via a forum centered on the cutting-edge techniques of today's toxicology trainees.

Introduction. Aaron Bowman, Vanderbilt University Medical Center, Nashville, TN.

Potential for Autophagy as a Primary Mechanism of Environmentally-Induced Neurodegeneration. Jason Cannon, Purdue University, West Lafayette, IN.

Autophagy: Friend or Foe in Arsenic-Induced Toxicity? Carla Garza-Lombo, University of Nebraska Lincoln, Lincoln, NE.

Role of Autophagy in Manganese-Induced Neurotoxicity. Ziyan Zhang, Albert Einstein College of Medicine, Bronx, NY.

Manganese Modifies the AKT/mTOR Pathway and Autophagy: Implications for Huntington's Disease Pathology. Miles Bryan, Vanderbilt University Medical Center, Nashville, TN.

Optineurin Is a Critical Player in Parkinson's Disease Pathogenesis. Johnny Wise, Purdue University, West Lafayette, IN.

Environmental Neurotoxic Pesticide Endosulfan Induces Autophagy Preceding Apoptotic Cell Death in Dopaminergic Neuronal Cells: Relevance to Etiopathogenesis of Parkinson's Disease. Adithiya Charli, Iowa State University, Ames, IA.

Dopaminergic Cell Recovery and Resilience *In Vitro*: The Role of Autophagy. Georgina Harris, Johns Hopkins Center for Alternatives to Animal Testing, Baltimore, MD.

The Role of the Epigenome in the Etiology of Metal-Induced Disease

Wednesday, March 14, 1:30 PM to 4:15 PM

Chairperson(s): *Rebecca Fry, University of North Carolina at Chapel Hill, Chapel Hill, NC; and Miroslav Styblo, University of North Carolina at Chapel Hill, Chapel Hill, NC.*

Primary Endorser:
Metals Specialty Section

Other Endorser(s):
Mechanisms Specialty Section
Reproductive and Developmental Toxicology Specialty Section

Toxic metals, such as arsenic, cadmium, lead, and mercury, represent a major public health threat for populations worldwide. Exposures to these metals can be through various sources, including, but not limited to, contaminated food and water. In terms of associated health effects, chronic exposure to toxic metals has been linked to cancers of numerous organs, including the lung, liver, and bladder. Toxic metals also are associated with non-cancer endpoints, such as adverse neurodevelopmental outcomes and cardiometabolic disease, including diabetes mellitus and cardiovascular disease in adults. Of particular concern are prenatal and early-life exposures to toxic metals that are associated with increased risk of low birth weight, preterm birth, susceptibility to infection, and later-life cancers. Among the many proposed cellular mechanisms that underlie toxic metals-associated disease are epigenetic modifications, including DNA methylation, histone modifications, and micro-RNA (miRNA) dysregulation. This symposium will highlight the complex role of the epigenome in the etiology of toxic metals-induced disease. The session speakers will present results from epigenomic studies spanning *in vitro* cell culture models, rodent models, and human populations exposed to toxic metals. The diseases of focus will include diabetes, developmental effects in children, and metabolic disorders related to exposures to arsenic, cadmium, lead, and mercury. The presentations will highlight the role of toxic metals as epigenetic modifiers of DNA methylation and miRNA expression and mediators of a panoply of diseases. The use of epigenetic data for risk assessment and disease risk prediction also will be discussed.

Prenatal Arsenic Exposure and the Epigenome: Informing Disease Mechanisms and the Risk Assessment Process. Rebecca Fry, University of North Carolina at Chapel Hill, Chapel Hill, NC.

The Role of microRNAs in the Etiology of Diabetes Associated with Chronic Exposure to Arsenic. Praveen Sethupathy, Cornell University, Ithaca, NY.

Epigenomic Effects of Cadmium on the Placenta Influence Newborn and Early-Childhood Growth. Carmen Marsit, Emory University, Atlanta, GA.

Mitochondria Direct Arsenic-Induced Epigenetic Regulation of Stem Cell Fate. Aaron Barchowsky, University of Pittsburgh, Pittsburgh, PA.

Epigenome-Wide Association Studies of Prenatal Metal Exposures in a Longitudinal Pre-Birth Cohort. Andrea Baccarelli, Columbia University, New York, NY.

Workshop Session

Microbiota as a Target or Mediator of Adverse Effects: Implications for Toxicology

Wednesday, March 14, 1:30 PM to 4:15 PM

Chairperson(s): *Bennard van Ravenzwaay, BASF, Ludwigshafen am Rhein, Germany; and Shana Sturla, ETH Zürich, Zürich, Switzerland.*

Primary Endorser:
Molecular and Systems Biology Specialty Section

Other Endorser(s):
Carcinogenesis Specialty Section
Reproductive and Developmental Toxicology Specialty Section

The microbiome has emerged as a key regulator of development and disease. A disruption in host-associated microbial communities is correlated with obesity, immune, and cardiovascular diseases and, increasingly, with adverse developmental outcomes. Current research is starting to unravel microbiome-host interactions that may explain these effects by examining microbiota as a target or mediator of chemical toxicity. One mechanism by which microbiota may modify toxicity is via chemical-dependent changes in the production of small molecules that disrupt normal biological processes in the host. Humans share 99.9% of their genome, yet the vastly larger microbiota-genomic space is much less conserved and, therefore, may partially explain inter-individual susceptibility to chemical exposures. Due to high inter- and intraspecies variability within microbiota and its responsiveness to external factors, it is essential to determine the effects of chemical exposures on gut microbiota composition, function, community organization, and resulting host-microbiota interactions. There also is a need to identify molecules produced by gut microbiota and their effects on the host, as well as understanding how xenobiotic compounds are biotransformed by resident microbiota. This mechanistically-focused session highlights emerging interactions between gut microbes and the host that contribute to altering exposure and susceptibility to drugs and chemicals. The first talk will provide an overview of the metabolic capacity of the gut microbiome and, using a combination of metagenomics, metabolomics, synthetic biology, and cutting-edge experimental host-microbiota model systems, reveal the metabolic characterization of individual microbial species and their roles in human biology and disease.

The second talk will focus on understanding the toxicological impact of chemical transformations of food carcinogens and how these reactions are mediated by microbial communities. The third presenter will describe an innovative zebrafish model to test whether host-associated microbiota modify the developmental neurotoxicity of environmental chemicals. The fourth presenter will discuss microbiota in the context of cancer therapeutics. The fifth talk will provide a framework for the assessment of risks associated with microbiome changes via the investigation of the microbiome's functionality, defined as the production of metabolites absorbed by the host. Hazard identification and risk assessment do not currently consider host-microbiota interactions that are disrupted by xenobiotic exposure. This session will bring together academic, government, and industry scientists who are using novel experimental systems to determine the composition and organization of gut microbiota. Relevant to the field of toxicology, the effects of chemical exposures on host-microbiome interactions and the mechanisms by which microbiota perform biotransformations of drugs and environmental chemicals will be discussed in this session.

Introduction. Bennard van Ravenzwaay, BASF, Ludwigshafen am Rhein, Germany

Metabolic Capability of the Gut Microbiome. Michael Fischbach, University of California San Francisco, CA.

Gut Microbial Transformations of Carcinogens and Their Toxicological Relevance. Shana Sturla, ETH Zürich, Zürich, Switzerland.

Environmental Chemicals Disrupt the Microbiota-Gut-Brain Axis during Zebrafish Development. Tamara Tal, US EPA, Research Triangle Park, NC.

Discovering and Controlling the Gut Microbiome's Impact on Xenobiotic Metabolism. Matthew Redinbo, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Influence of the Microbiome on Plasma Metabolite Patterns: Can Microbiome Changes Be Detected by Metabolomics? Christina Behr, BASF and Wageningen University & Research, Ludwigshafen am Rhein, Germany

Regional Interest Session

Toxicology and Public Health Solutions for Environmental Emergency-Related Contamination Events

Wednesday, March 14, 1:30 PM to 4:15 PM

Chairperson(s): *Ivan Rusyn, Texas A&M University, College Station, TX; and Michael Honeycutt, Texas Commission on Environmental Quality (TCEQ), Austin, TX.*

Primary Endorser:
Specialty Section Collaboration and Communication Group

Other Endorser(s):
Mixtures Specialty Section
Regulatory and Safety Evaluation Specialty Section

Climate change and shifts in domestic economic activity markedly increase risks from catastrophic chemical contamination events resulting from weather-related or anthropogenic emergencies. These events are especially acute in the coastal areas, and Texas represents a region where many past and recent events demonstrated an acute need to characterize and manage both existing and environmental emergency-created hazardous waste sites through the development of the tools that can be used by first responders, the impacted communities, and the government bodies involved in site management and cleanup. The complexities of hazardous chemical exposures, potential adverse health impacts, and the need to rapidly and comprehensively evaluate the potential hazards of exposures to complex mixtures during emergency events create unique challenges in toxicology and public health. This session will bring together a diverse set of governmental, academic, and industry stakeholders to highlight solutions and research strategies that are available today for disaster research and response. Approaches that span from computational tools to novel *in vitro* models to population-based human studies of exposure and adverse health effects will be highlighted to present a range of options that are either already available and have been implemented or are on the short-term horizon. Design and implementation of comprehensive solutions for complex exposure- and hazard-related challenges is a goal for environmental health that aims to protect the communities and infrastructure that are vulnerable to major weather-related events.

Unique Challenges in Environmental Emergency Preparedness and Response in the Coastal Areas. Michael Honeycutt, Texas Commission on Environmental Quality (TCEQ), Austin, TX.

Deep Water Horizon Oil Spill—Lessons Learned in Applying Novel Assessment Methodologies in Emergency Response. Richard Judson, US EPA, Research Triangle Park, NC.

Designing Effective Rapid Toxicological Research in Response to Environmental Public Health Disasters. Scott Masten, NIEHS, Research Triangle Park, NC.

Rapid Estimation of Hazard and Risk Using Computational Tools. Jessica Wignall, ICF International, Inc., Fairfax, VA.

Novel Approaches to Rapid and Informative Exposure Analysis from Environmental Samples and Mixtures. Erin Baker, Pacific Northwest National Laboratory, Pasco, WA.

Population-Based Studies before, during, and after Emergencies—Building Resilience in Coastal Communities. Jennifer Horney, Texas A&M University, College Station, TX.

Roundtable Session

The Kinetically-Derived Maximum Dose (KMD), a New Dimension to the Maximum Tolerated Dose (MTD)

Wednesday, March 14, 4:30 to 5:50 PM

Chairperson(s): *Jeanne Domoradzki, The Dow Chemical Company, Midland, MI; and Alan Boobis, Imperial College London, London, United Kingdom.*

Primary Endorser:
Regulatory and Safety Evaluation Specialty Section

Other Endorser(s):
Risk Assessment Specialty Section

Evaluations of chemicals tested under dose-selection protocols using a maximum tolerated dose (MTD) design (e.g., decreased body weight and/or histological injury) are increasingly revealing that interpretation is confounded by the onset of non-dose-proportionate systemic dose (i.e., nonlinear toxicokinetics). This is due to saturated absorption, distribution, and metabolism and/or clearance mechanisms of parent chemical and/or metabolites. Recent toxicity testing guidance from the Organisation for Economic Co-operation and Development (OECD) and US Environmental Protection Agency (US EPA) and other evaluations from the National Academy of Sciences (NAS) and ILSI Health and Environmental Sciences Institute (HESI) have clearly indicated that toxicity observed only under nonlinear toxicokinetic conditions often has limited, if any, quantitative relevance to risks to human health if the onset of dose-non-proportionality is well separated from real-world human exposures. Detection of nonlinear toxicokinetics has been improved by analytical techniques/approaches that have made assessment of systemic/internal dose in test animals substantially more sensitive, lower cost, and higher throughput. In addition, determination of whether the onset of toxicokinetic nonlinearity is well separated from human exposure is increasingly possible given rapid improvements in modeling and/or analytical biomonitoring analyses supporting human environmental-exposure assessments. Saturation of any biological process should be evaluated for its relevance to dose-response relationships relative to human exposure. Systemic dose non-proportionality should not be treated any differently from toxicity findings due to excessive stress indicated by the conventional MTD approach. Use of evidence of dose non-proportionality for selection of an acceptable top dose for animal toxicity testing has been termed the kinetically-derived maximum dose (KMD). Despite the convergence of these indisputable advances, however, current toxicity test protocols and interpretation of existing toxicity test findings continue to be largely dominated by long-ingrained concepts of conventional MTD thinking. Current toxicity test dose selection often is conducted oblivious to a prior evaluation of toxicity at internal non-dose-dependent metrics, and conversely, extensive, costly, and animal-intensive post hoc mode-of-action analyses are frequently implemented to address high-dose specific toxicity findings that could (should) otherwise be ruled out as quantitatively non-human relevant on systemic dose alone. Thus, effective implementation of the fundamental toxicology principle of "the dose makes poison" must include an ever-expanding commitment to consideration of animal and human internal dose evaluations as a key part of chemical risk assessment. The rapid expansion of analytical technologies, exposure assessments, and reducing the use of animals demands nothing less. The objective of this session is to catalyze understanding and discussion surrounding the use of systemic dose kinetics in selection of improved human-relevant doses in animal toxicity testing and/or retroactive interpretation of high-dose specific toxicity findings in evidence-based human risk assessments. The presentations will address: 1) a review of background and biological mechanisms accounting for non-linear responses in toxicity studies; 2) the KMD, conceptualization and mechanisms for experimental identification; 3) application of KMD principles to post hoc interpretation of high-dose specific toxicity studies; and 4) regulatory perspectives on use of findings at non-dose-proportional doses in human risk assessment. The roundtable discussion between speakers and the audience will address the implications of KMD-based assessments for the practice of toxicology and risk assessment, such as: 1) the KMD as a replacement for the MTD; 2) research and policy constraints in the use KMD; 3) adequacy of existing regulatory toxicity testing guidance and protocol design (e.g., toxicokinetics to support KMD evaluations); 4) offering an alternative to conducting conventional high-dose specific mode-of-action investigations; 5) assisting design and interpretation of adverse outcome pathway (AOP)/mode-of-action studies; and 6) informing life-stage-specific differences in toxicity.

Introduction. Jeanne Domoradzki, The Dow Chemical Company, Midland, MI.

The Mechanistic Basis of Non-Proportionate Systemic Doses in Toxicology Studies and Implications for Chemical Risk Assessment. Alan Boobis, Imperial College London, London, United Kingdom.

Use of KMD in Regulatory-Mandated Toxicity Testing of Non-Pharmaceuticals: From Concept to Application. Shakil Saghir, Smithers Avanza, Gaithersburg, MD.

Kinetically-Derived Maximum Dose: A Key Initiating Event Impacting Need for Mode-of-Action Investigations of High-Dose Specific Toxicity. James Bus, Exponent, Midland, MI.

Regulatory Perspectives on the Use of Toxicokinetic Data in Human Risk Assessment. Anna Lowit, US EPA, Washington, DC.

Informational Session

The US Tox21 Collaboration: A Decade of Experience and a New Vision for the Future

Wednesday, March 14, 4:30 PM to 5:50 PM

Chairperson(s): *Bette Meek, University of Ottawa, Ottawa, ON, Canada; and Kevin Crofton, US EPA, Research Triangle Park, NC.*

Primary Endorser:
Carcinogenesis Specialty Section

Other Endorser(s):
***In Vitro* and Alternative Methods Specialty Section**
Molecular and Systems Biology Specialty Section

In 2007, Tox21 was launched as a multi-agency collaborative effort among the National Institutes of Health (NIH)'s National Institute of Environmental Health Sciences (NIEHS, National Toxicology Program (NTP), and the National Center for Advancing Translational Sciences (NCATS); the US Environmental Protection Agency (US EPA)'s National Center for Computational Toxicology (NCCT); and the US Food and Drug Administration (US FDA). The objective of this partnership was to shift the assessment of chemical hazards from traditional experimental animal toxicology studies to one based on target-specific, mechanism-based, *in vitro* assays, with the ultimate aim of improving human and environmental risk assessments. In this regard, the collaborative was highly successful in that thousands of chemicals have been screened in hundreds of bioassays. These data have been publicly released for consideration and use in a range of contexts, including regulatory decisions. However, complex challenges remain. The intent of this symposium is to review the 2017 strategic plan for Tox21 and gain feedback from the diverse stakeholders at SOT. The new strategic plan promotes: 1) addressing key limitations in *in vitro* assays; 2) continued development and use of alternative test systems that predict human toxicity; 3) management and curation of large chemical libraries; 4) curation of legacy *in vivo* toxicity studies; 5) performance-based validation of high-throughput *in vitro*, *in silico*, stem cell and microphysiological systems, and other emerging technologies; and 6) development and use of *in vitro* methods for characterizing pharmacokinetics. Each of the speakers will summarize lessons learned and outline their agency's approaches aimed at solving complex challenges. The strategy embraces transparency and technological change, aims to protect human health environment, with an ultimate goal of fostering broader acceptance of alternative data streams in regulatory decisions.

A New Tox21 Strategic Plan and the Integration of EPA Science. Russell Thomas, US EPA, Research Triangle Park, NC.

Evolution of Tox21 High-Throughput Screening: Accomplishments and New Strategic Directions. Anton Simeonov, NCATS, Rockville, MD.

The Future of Tox21: Changing the NTP Landscape. Richard Paules, NIEHS, Research Triangle Park, NC.

Determining the Predicative Ability of *In Vitro* Microphysiological Systems to Answer Critical Regulatory Questions. Suzanne Fitzpatrick, US FDA, College Park, MD.

Validation for 21st-Century Science. Warren Casey, NTP NICEATM, Research Triangle Park, NC.

Education-Career Development Session

Research-Based Approaches to Improve Teaching Effectiveness in Toxicology Classrooms

Wednesday, March 14, 4:30 PM to 5:50 PM

Chairperson(s): *Barbara Kaplan, Mississippi State University, Mississippi State, MS; and Larissa Williams, Bates College, Lewiston, ME.*

Primary Endorser:
Education Committee

Other Endorser(s):
Career Resource and Development Committee
Postdoctoral Assembly

Teaching students effectively at all levels in science requires continuous learning on the part of the instructor. Not only is content knowledge increasing, so are the tools to teach it. At the heart of pedagogy, though, is research about how students learn to maximize educational outcomes and retention. While lecturing has been the predominant method of instruction since the founding of universities, there is evidence to suggest that this is not the most effective way to teach. Through national initiatives such as the National Science Foundation's Vision and Change in Undergraduate Biology Education, research-based teaching methods are having a growing impact in higher education. This session will bring together educators to talk about best practices in student-centered teaching that are applicable to all educational levels. The topics to be discussed include: 1) an introduction to designing course methods, assignments, and assessments to optimize students' opportunities to learn; 2) lessons learned from a flipped classroom; 3) the use of problem formulation and experimental design in the context of a graduate immunotoxicology classroom; 4) how community-engaged learning and research can improve comprehension, recruitment, and retention; and 5) case studies from industry to teach about risk communication. This session will conclude with time for questions, giving audience members an opportunity to further explore these and other related topics. This session will be of interest to current educators and those interested in teaching, such as graduate students and postdocs.

Introduction. Larissa Williams, Bates College, Lewiston, ME.

Scientific Teaching: Using the Rigor of Science to Facilitate Learning in the Classroom. Edwin Barea-Rodriguez, University of Texas at San Antonio, San Antonio, TX.

Lessons Learned from a Flipped Classroom. Larissa Williams, Bates College, Lewiston, ME.

Graduate Toxicology Presented in the Context of Problem Formulation and Experimental Design. Barbara Kaplan, Mississippi State University, Mississippi State, MS.

Taking the Student Out of the Classroom with Community-Engaged Learning and Research. Christian Curran, Northern Kentucky University, Highland Heights, KY.

Effective Communication of Toxicology Principles Is Critical to the Industry Toxicologist. Steven Hermansky, ConAgra Foodservice, Omaha NE.

Symposium Session

In Vitro Test Methods to Model Local Respiratory Effects after Exposure to Pulmonary Toxicants: Not Just Smoke and Mirrors

Thursday, March 15, 8:30 AM to 11:15 AM

Chairperson(s): *Holger Behrsing, Institute for In Vitro Sciences, Gaithersburg, MD; and Mark Higuchi, US EPA, Research Triangle Park, NC.*

Primary Endorser:
***In Vitro* and Alternative Methods Specialty Section**

The lungs are exposed to a wide range of toxicants, including environmental, pharmaceutical, and occupational. Evaluating this assortment of toxicants has necessitated the development of physiologically-relevant *in vitro* models. These *in vitro* models have proven to be sensitive, robust, reproducible, and capable of providing a diverse outcome of responses. These responses focus on inflammation characterized by cytokine secretion, mucus production, goblet cell hyperplasia, and increased ciliary beat frequency. This session will explore recent findings in *in vitro* toxicology that link a variety of pulmonary toxicants with their common inflammatory outcomes. The first speaker will focus on *in vitro* pulmonary models and their incorporation into a testing scheme. In the second presentation, a comparison of cell lines to 3D air-liquid interface (ALI) will be detailed. The third speaker will discuss *in vivo-in vitro* comparisons, as well as 3D ALI. The fourth speaker will demonstrate dosimetry modeling of *in vitro* e-cigarette exposure. Speaker five will reveal the factors that must be taken into account for proper *in vitro* exposure modeling. Further comparisons between different *in vitro* exposure systems will be explained by speaker six. Finally, the last speaker will lay out the requirements to achieve *in vitro* testing regulations and the role each sector must play in achieving regulation.

These speakers, who come from a mix of government and industry backgrounds, demonstrate how a range of pulmonary exposures can be evaluated using *in vitro* methods for detecting local respiratory effects and the steps necessary to establish regulations for these testing methods.

Introduction. Holger Behrsing, Institute for In Vitro Sciences, Gaithersburg, MD.

Modern *In Vitro* Test Systems Provide Human-Relevant Toxicity Data to Support Product Development and Regulatory Decision Making. Holger Behrsing, Institute for In Vitro Sciences, Gaithersburg, MD.

***In Vivo-In Vitro* Comparison of Acute Respiratory Tract Toxicity Using Different 2D and 3D Models and a Successful Example Using Physico-Chemical Characteristics of the Test Substance.** Robert Lansiedel, BASF, Ludwigshafen am Rhein, Germany.

The Challenge of Integrating Non-Animal Alternative Approaches to Assess the Risk to Human Health from Inhaled Materials. Jon Hotchkiss, The Dow Chemical Company, Midland, MI.

***In Vitro*/*Ex Vivo* Exposure System Dosimetry: Successes and Challenges.** Mike Oldham, Altria Client Services, Richmond, VA.

Operating Procedures to Improve Efficiencies of *In Vitro* Exposure Systems at the Air-Liquid Interface. Mark Higuchi, US EPA, Research Triangle Park, NC.

Understanding Air-Liquid Interface Cell Exposure Systems: A Comprehensive Assessment of Various Systems under Identical Conditions. Jose Zavala, US EPA, Research Triangle Park, NC.

Novel Non-Animal Respiratory Test Methods Show Great Promise, So How Do We Get Them into Routine Use: Points to Consider for Industrial and Regulatory Acceptance. Hans Raabe, Institute for In Vitro Sciences, Gaithersburg, MD.

Workshop Sessions

A Search for Biomarkers of Neurotoxicity: A Practical Approach

Thursday, March 15, 8:30 AM to 11:15 AM

Chairperson(s): *David Herr, US EPA, Research Triangle Park, NC; and Michael Aschner, Albert Einstein College of Medicine, Bronx, NY.*

Primary Endorser:
Neurotoxicology Specialty Section

Other Endorser(s):
Clinical and Translational Toxicology Specialty Section
Regulatory and Safety Evaluation Specialty Section

Human exposures to drugs, chemicals, and chemical mixtures often are associated with symptoms suggestive of nervous system involvement (headache, fatigue, cognitive changes, etc.), yet broadly applicable screening methods to assess the neurotoxic condition in animal models are lacking. Thus, there is a need for more sensitive and specific biomarkers that can help diagnose and predict neurotoxicity that are relevant across animal models and translatable to the clinic. Fluid-based biomarkers, such as those found in serum, plasma, urine, and cerebrospinal fluid, have great potential due to the relative ease of sampling, but at present, data on their expression and translation are lacking or inconsistent. In order to identify such novel fluidic biomarkers associated with the development and expression of neurotoxicity and to evaluate their relative sensitivity with established phenotypic anchors of neurotoxicity, a pilot study was designed under the auspices of the ILSI Health and Environmental Sciences Institute (HESI) Technical Committee on Translational Biomarkers of Neurotoxicity—members include representatives from academia, industry, and government. Trimethyltin (TMT) was selected as a prototypic compound since relevant data are available on dose response, time course, and site of action. Neuropathology was confirmed by traditional histopathological assessments, behavioral changes, and alterations in neurochemical and neuroinflammatory biomarkers in brain areas targeted by a single dose of TMT (7.0 mg/kg body weight) at two, six, 10, and 14 days. Using state-of-the-art assessment techniques, the researchers identified specific biological chemicals or patterns of biological chemicals in serum, plasma, or cerebral spinal fluid that are associated with nerve cell damage/degeneration caused by TMT. Such changes include alterations in the status of the metabolome and the expression of microRNAs, as well as levels of interleukins and other related circulating antigen factors. Histopathological assessments of TMT effects in select non-brain tissues enabled improved interpretation of the brain specificity of these changes. Correlation of high-throughput endpoints with markers of neurotoxicity, especially glial fibrillary acid protein, neuropathological loss of neurons, and oxidative damage to neurons as presented here provide a guideline by which to establish fluidic biomarkers of neurotoxicity. The data from this pilot study also will help design follow-on studies utilizing other known neurotoxicants to determine the generalizability of the findings in an effort to develop and validate a set of biochemical markers of neurotoxicity that will be accessible clinically. Such clinical biomarkers should prove valuable to research ranging from preclinical studies to clinical trials and assist with the monitoring of the severity of and recovery from brain injury.

Introduction. David Herr, US EPA, Research Triangle Park, NC.

Overview of the Biomarker Initiative to Identify Biological Fluid-Based Indicators of Neurotoxicity. William Slikker Jr., NCTR, Jefferson, AR.

Glial Fibrillary Acidic Protein (GFAP) and Related Astroglial Proteins as Biomarkers of Neurotoxicity. James O'Callaghan, NIOSH, Morgantown, WV.

Changes in the Metabolome May Serve as Peripheral Biomarkers of CNS Toxicity. David Herr, US EPA, Research Triangle Park, NC.

Neurotoxicant Effects on Non-Brain Tissues: Understanding Biomarker Specificity. Ingrid Pardo, Pfizer, Inc., Groton, CT.

Biochemical and Molecular Endpoints as Biomarkers of Neurotoxicity and Their Correlation with Neuropathological Damage. Syed Imam, NCTR, Jefferson, AR.

Workshop Discussion. Abby Li, Exponent, Oakland, CA; and Allison Harrill, NIEHS, Research Triangle Park, NC.

Deliberations in Regulatory and Safety Assessment of Food Substances in Early Life

Thursday, March 15, 8:30 AM to 11:15 AM

Chairperson(s): *Wallace Hayes, Harvard University, Cambridge, MA, and Michigan State University, East Lansing, MI; and Brinda Mahadevan, Abbott Laboratories, Mumbai, India.*

Primary Endorser:
Regulatory and Safety Evaluation Specialty Section

Other Endorser(s):
Food Safety Specialty Section
Women in Toxicology Special Interest Group

Neonates and younger children have a greater degree of vulnerability from consuming food than older children and adults. Much of this vulnerability is due to higher consumption per kilogram body weight. In comparison to adult dietary patterns, neonates and younger children's food behavior is largely atypical. It also is important to remember that neonates and younger children are in a rapidly developing phase of their life cycle when most organs are still developing and differentiating, leaving them in a potentially vulnerable state regarding ingredients and foods consumed. For the most part, regulatory guidelines for foods and food ingredients are in place; however, in the case of neonates and very young children, deliberation regarding the need for additional information to ensure the safety of food ingredients in early life is an area of ongoing discussion. The current paradigm for safety characterization of an ingredient for use in infant formula is, for the most part, limited to chemical characterization, anticipated exposure levels, and data from nonclinical and clinical studies. Additionally, acceptable daily intakes (ADIs) currently do not apply to infants less than 12 weeks of age. The scientific community is pondering the need for a paradigm shift in the regulation of ingredients added to infant formula consumed in early stages of life. The objectives of this workshop are to address: 1) the need to derive a holistic understanding of exposure to ingredients in food during early stages of life and its associated toxicities with special emphasis on neonatal biology; 2) if there are key elements needed beyond the currently required toxicological studies to enable decision making on the adequacies or inadequacies of existing ADIs in early stages of life; 3) what the age-specific factors are that need to be considered in developing kinetic models for early stages of life and how normal inter-individual and other sources of variability should be included in modeling predictions, and 4) if there are any differences and similarities in the safety assessment strategies that are in place for the safety of ingredients in early stages of life and how these uncertainties impact regulatory decision making.

Does Infant Exposure Matter in Safety Assessment? Wallace Hayes, Harvard University, Cambridge, MA, and Michigan State University, East Lansing, MI.

Applying Concepts of Life Stage for Safety Assessment and Understanding the Needs for Children. Elaine Faustman, University of Washington, Seattle, WA.

Integrated Safety Assessments of Food Additives in Early Life. Anne Constable, Nestlé Research Centre, Lausanne, Switzerland.

Threshold of Toxicological Concern (TTC) Versus Other Methods in Risk Assessment of Food Constituents. Dieter Schrenk, Technische Universität Kaiserslautern, Kaiserslautern, Germany.

Regulatory Toxicology Challenges in Life Stage-Specific Safety Assessments. April Neal-Kluever, US FDA, Washington, DC.

Nonclinical to Clinical Translation of Antibody-Drug Conjugates

Thursday, March 15, 8:30 AM to 11:15 AM

Chairperson(s): *Subramanya (Subbu) Karanth, Medimmune, Gaithersburg, MD; and Amy Sharma, Amgen, Seven Oaks, CA.*

Primary Endorser:
Biotechnology Specialty Section

Other Endorser(s):
Clinical and Translational Toxicology Specialty Section
Regulatory and Safety Evaluation Specialty Section

Antibody drug conjugates (ADCs) are a rapidly growing class of targeted anticancer therapeutics that now account for a significant fraction of pharmaceutical pipelines. Despite initial clinical success and marketing approvals of Kadcyla and Adcetris, clinical development continues to be impeded by safety issues. Of the greater than 50 ADCs evaluated in early clinical trials, approximately 20 have been discontinued due to lack of efficacy and/or intolerable toxicity. Significant efforts to overcome these hurdles are currently underway, including engineering efforts to develop next-generation molecules with different mechanisms of action and superior conjugation stability. In addition to technology advances, there also is a significant need to develop translational strategies to optimize the therapeutic window and decrease the rate of attrition for novel ADCs. The purpose of this session is to bring together experts to discuss recent progress and challenges in the design and development of ADCs. The session will explore strategies for preclinical safety assessment that can be used to improve therapeutic indices of next-generation ADCs.

Introduction and Overview. Subramanya (Subbu) Karanth, Medimmune, Gaithersburg, MD.

Translational Value of Nonclinical Safety Studies. Nicola Stagg, Genentech, Inc., San Francisco, CA.

Safety Perspectives Including Class Effects and Off-Target Toxicity. Haley Neff-LaFord, Seattle Genetics, Bothell, WA.

A Regulatory Update on Nonclinical Expectations to Support the Safety of ADCs. Whitney Helms, US FDA, Silver Spring, MD.

Translational Strategies to Maximize Therapeutic Index of ADCs. Mary Jane Hinrichs, Medimmune, Gaithersburg, MD.

Informational Session

The NIEHS Nanotechnology Health Implications Research (NHIR) Consortium

Thursday, March 15, 8:30 AM to 11:15 AM

Chairperson(s): *Srikanth Nadadur, NIEHS, Research Triangle Park, NC; and Robert Tanguay, Oregon State University, Corvallis, OR.*

Primary Endorser:
Nanotoxicology Specialty Section

The widespread use of engineered nanomaterials (ENMs) in consumer products is a concern for potential unintended exposure to ENMs and the impact on health. The overarching goal of the National Institute of Environmental Health Sciences (NIEHS) Nano Environmental Health and Safety (Nano EHS) program is to gain fundamental understanding of the molecular and pathological pathways implicated in potential adverse health effects of ENMs. In the absence of an identified pathology associated with ENMs, the NIEHS took a proactive approach aimed at developing an ENMs-biological interactions knowledge base, based on physicochemical properties of ENMs. This comprehensive knowledge base is hoped to guide and develop *in silico* approaches for human health risk characterization and potential intervention or remedial measures, as well the design of benign nanomaterials. The NIEHS recognized the need to promote collaborative team science efforts to address the multidisciplinary nature of assessing ENMs on environmental health and safety. Towards this goal, based on the past two decades of promoted research through the Nano GO Consortium and NIEHS Centers for Nanotechnology Health Implications Research (NCNHIR) and the research outcomes from these efforts, the NIEHS Nanomaterials Health Implications Research (NHIR) Consortium was established in 2016. This consortium will expand the library of ENMs and physico-chemical properties focusing on specific materials with high production and use in consumer products, as well as recently emerging 2D and 3D ENMs containing new transitional metals and whose toxicology is unknown at the nanoscale.

The comprehensive toxicological profile for these ENMs surveyed using a wide range of systems reflecting more physiologically relevant models will benefit the future goals of this program (i.e., to promote computational modeling efforts to predict association between ENM physicochemical properties and potential health effects).

Introduction. Srikanth Nadadur, NIEHS, Research Triangle Park, NC.

Engineered Nanomaterial Synthesis, Characterization, and Method Development Center for Nano-Safety Research. Philip Demokritou, Harvard T.H. Chan School of Public Health, Boston, MA.

Key Events in Modulation of Lung Infection Susceptibility by Engineered Nanomaterials. Brian Thrall, Pacific Northwest National Laboratory, Richland, WA.

Analytical Assessment of Protein Conformational Change Induced by Interaction with Nanomaterials. Wenwan Zhong, University of California Riverside, Riverside, CA.

Multidimensional *In Vivo* Assessments of Engineered Nanomaterials and Biological Interactions. Robert Tanguay, Oregon State University, Corvallis, OR.

Biological Response Profiles of Selected Engineered Nanomaterials after Perinatal Exposure. Peter Thorne, University of Iowa, Iowa City, IA.

Toxicological Profiling of Engineered Nanomaterials in the Mononuclear Phagocyte System in the Liver and the Immune System. Tian Xia, University of California Los Angeles, Los Angeles, CA.

Toxicity of Metallic Engineered Nanomaterials to Corneal Epithelial Cells. Soohyun Kim, University of California Davis, Davis, CA.

Impact of Early-Life Exposure to Engineered Nanomaterials. Timothy Fennell, RTI International, Research Triangle Park, NC.

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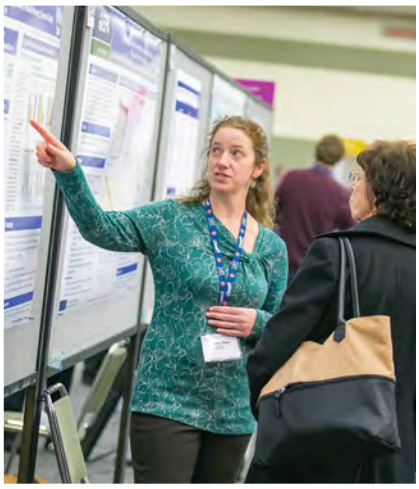
December 5, 2017–January 12, 2018

Cost: $75 per abstract

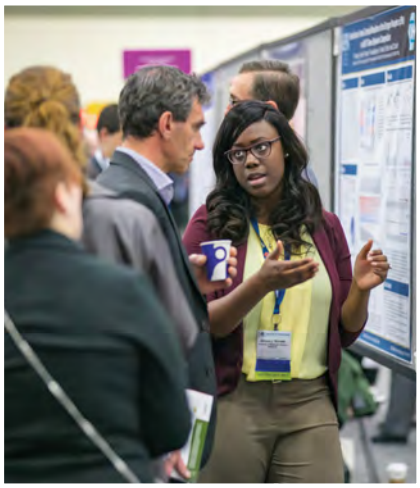


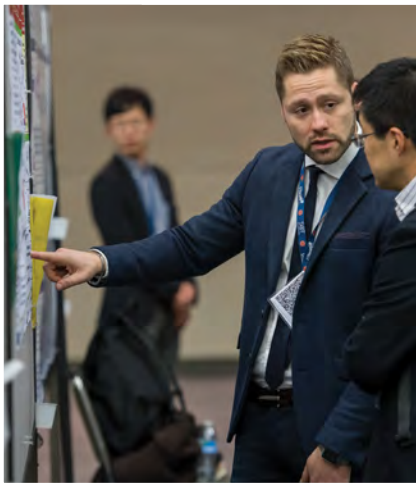
Important Reminders:

Late-breaking abstracts should represent new research—not a revision of a previously submitted abstract. They should describe high-impact, original research that could not be completed prior to the original abstract deadline.

Late-breaking abstracts will be programmed on Thursday, March 15. They are reviewed by the Scientific Program Committee and evaluated by the same standards as abstracts submitted for the original deadline.

Accepted late-breaking abstracts will be provided as a PDF addendum to *The Toxicologist* and are accessible through the SOT Mobile Event App and Online Planner.





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The exhibitors are constantly looking to add talented individuals to their team. A space solely focused on toxicology is the perfect environment to flex your networking skills by shaking hands and rubbing shoulders with industry leaders!

Don't forget! ToxExpo also is the location of poster presentations, food vendors, and comfortable seating and power stations to recharge you and your device. Come see it all!

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Exhibitor-Hosted Sessions

Monday

Releasing the Immune System Brakes: The Importance of Modeling Effects in Nonclinical Safety Studies

Monday, March 12, 9:00 AM to 10:00 AM

Presented by: *Envigo*

Checkpoint inhibitors release the immune system's biological control mechanisms, increasing anti-tumor activity. As these products enter the clinic, increasingly in combination with other drugs, it is essential to understand potential risks. Design of appropriate nonclinical studies, interpretation of results, and translation to the clinic are critical to understanding potential impact.

A New Telemetry-Based System for Assessing Cardiovascular Function in Large Animals—Part II, Pharmacological Validation by M. Markert, Boehringer Ingelheim

Monday, March 12, 10:30 AM to 11:30 AM

Presented by: *TSE Systems*

A first pharmacological evaluation of a newly-developed total implant telemetry system for cardiovascular, electrophysiological, and body temperature measurement. It is intended to be used for drug candidate safety pharmacological evaluations.

Implementation of Liquid Chromatography-Mass Spectrometric Workflows for the Quantitation of Large Molecule Biotherapeutics

Monday, March 12, 10:30 AM to 11:30 AM

Presented by: *Altasciences Clinical Research*

This session will outline workflows implemented using immunocapture-liquid chromatography mass spectrometry assays, high-resolution mass spectrometry, nano- and microflow chromatographic separation, and microsampling to expedite bioanalysis of large molecule biotherapeutics, including monoclonal antibodies, fusion proteins, and peptides. Case studies highlighting scientific considerations and regulatory challenges will be presented.

New Regulatory Drivers for Agrochemical Testing

Monday, March 12, 10:30 AM to 11:30 AM

Presented by: *Charles River*

New data requirements have been set for European agrochemical Regulations 283/2013 and 284/2013. Affecting such studies as *in vitro* metabolism, toxicokinetics, phototoxicity, immunotoxicity, and others, the requirements have shifted the agrochemical framework toward a more pharma-based development process.

Skin Sensitization: What Place Does *In Silico* Have within a Defined Approach?

Monday, March 12, 10:30 AM to 11:30 AM

Presented by: *Lhasa Limited*

Testing strategies incorporating *in silico* predictions can provide additional value by considering factors such as metabolism, lipophilicity, and chemical reactivity. Lhasa Limited will describe a defined approach integrating Derek Nexus with non-animal assays to reliably predict skin sensitization, and will compare its performance to both human and animal data.

Evolution of 3D Tissue Models for Toxicology and Disease Modeling

Monday, March 12, 12:00 Noon to 1:00 PM

Presented by: *Bio-Techne*

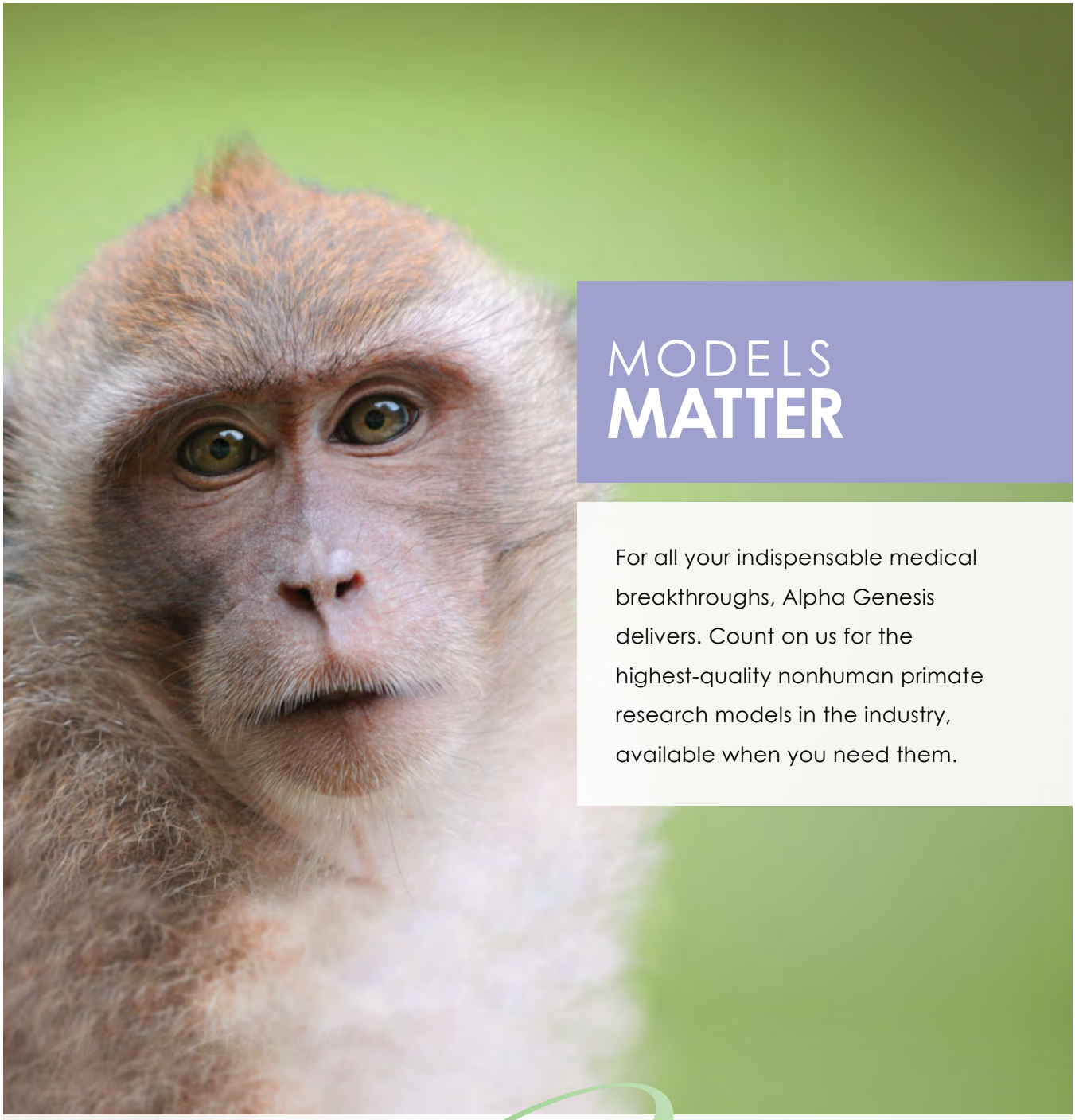
This session will present the history of *in vitro* models for toxicology, drug screening, and disease modeling. It will emphasize culture methods, advantages, and disadvantages of current 3D models. It will introduce MimEX™ Tissue Model Systems, a platform to generate sustainable, accessible, and physiologically-relevant 3D organ tissue on a 2D surface.

Leveraging Genetic Diversity to Reduce Clinical Attrition: A Novel Approach to *In Vitro* Safety and Toxicity Testing

Monday, March 12, 12:00 Noon to 1:00 PM

Presented by: *Coyne Scientific, LLC*

Coyne Scientific, a biotech services company, invites you to discover how using hiPSC-derived cardiomyocytes obtained from a cohort of genetically diversified individuals (rather than a single individual) can significantly improve the assessment of cardiac toxicity of pharmaceuticals within a target population and potentially reduce attrition of compounds in clinical development.



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10TH ANNIVERSARY

Neurotox and Cardiac Safety Assessment: Case Studies Employing iPS Cell Lines and Next-Generation MEA Technology

Monday, March 12, 12:00 Noon to 1:00 PM

Presented by: *Axion BioSystems and Cellular Dynamics International, a FUJIFILM company*

Discover the predictive power of iCell Cardiomyocytes^2 and iCell GlutaNeurons with the Maestro Pro multiwell MEA platform. Experts in the field will present case studies on optimization of neuronal/astrocyte co-culture for neurotoxicology (HESI NeuTox) and incorporation of the local extracellular action potential (LEAP) signal for cardiac safety (CiPA).

Tools for Streamlining QSAR/PBPK/QST Modeling and Simulation

Monday, March 12, 12:00 Noon to 1:00 PM

Presented by: *Simulations Plus, Inc.*

Simulations Plus and DILIsym Services have partnered to combine top-ranked, easy-to-use software (GastroPlus™, ADMET Predictor™, and DILIsym®) to streamline QSAR/PBPK/QST modeling and simulation in animals and humans, following administration around the body, and predict exposure/safety characterization of compounds in preclinical and clinical development. In this session, case studies will be presented demonstrating the integrated workflow to support research activities and regulatory submissions. Lunch will be provided.

Can Pharmacokinetic Modeling Keep Up with Risk Assessment in the 21st Century?

Monday, March 12, 1:30 PM to 2:30 PM

Presented by: *ScitoVation*

This session will explore current issues and future challenges associated with the increased requirement for rapid pharmacokinetic modeling associated with Tox21, the Lautenberg Chemical Safety Act, and animal welfare concerns. It will feature panel discussions with audience participation to discuss issues such as modeling platforms, model evaluation, and modeler training.

Immunopharmacology and Immunotoxicology in Minipigs in Support of Nonclinical Drug Development

Monday, March 12, 1:30 PM to 2:30 PM

Presented by: *Sinclair Research Center*

This session will describe how to develop, validate, and implement the different assays needed to support immunotoxicoloy investigations in minipigs. The design of special immunotoxicity studies for different breed of minipigs (Yucatan, Hanford, Sinclair, and Göttingen) and the collection and interpretation of immunotoxicology data in minipigs will be discussed.

Novel MetMax Hepatocytes and Enterocytes for the Evaluation Drug Metabolism, Drug-Drug Interactions, and Metabolism-Dependent Toxicity

Monday, March 12, 1:30 PM to 2:30 PM

Presented by: *In Vitro ADMET Laboratories*

MetMax™ hepatocytes and enterocytes are permeabilized cells supplemented with metabolic cofactors that have complete metabolizing enzyme pathways but can be stored and used like cell free fractions. Applications include metabolism, drug-drug interactions, and as exogenous metabolic activating systems for *in vitro* toxicity assays involving target cells incompetent in xenobiotic metabolism.

Validation of 3D Human Liver Microtissues for Enhanced DILI Prediction and Investigation of Mechanisms of Hepatotoxicity

Monday, March 12, 1:30 PM to 2:30 PM

Presented by: *InSphero Inc.*

3D microtissues have emerged as promising tools to assess mechanisms of hepatotoxicity, as they demonstrate enhanced liver phenotype and function. This session will present the most comprehensive evaluation by pharma to date, demonstrating their utility for enhanced DILI prediction, as well as application examples for studying mechanistic aspects of hepatotoxicity.

Genetic Diversity for Patient Specific Safety Assessments: Future of Toxicology?

Monday, March 12, 3:00 PM to 4:00 PM

Presented by: *Nanion Technologies*

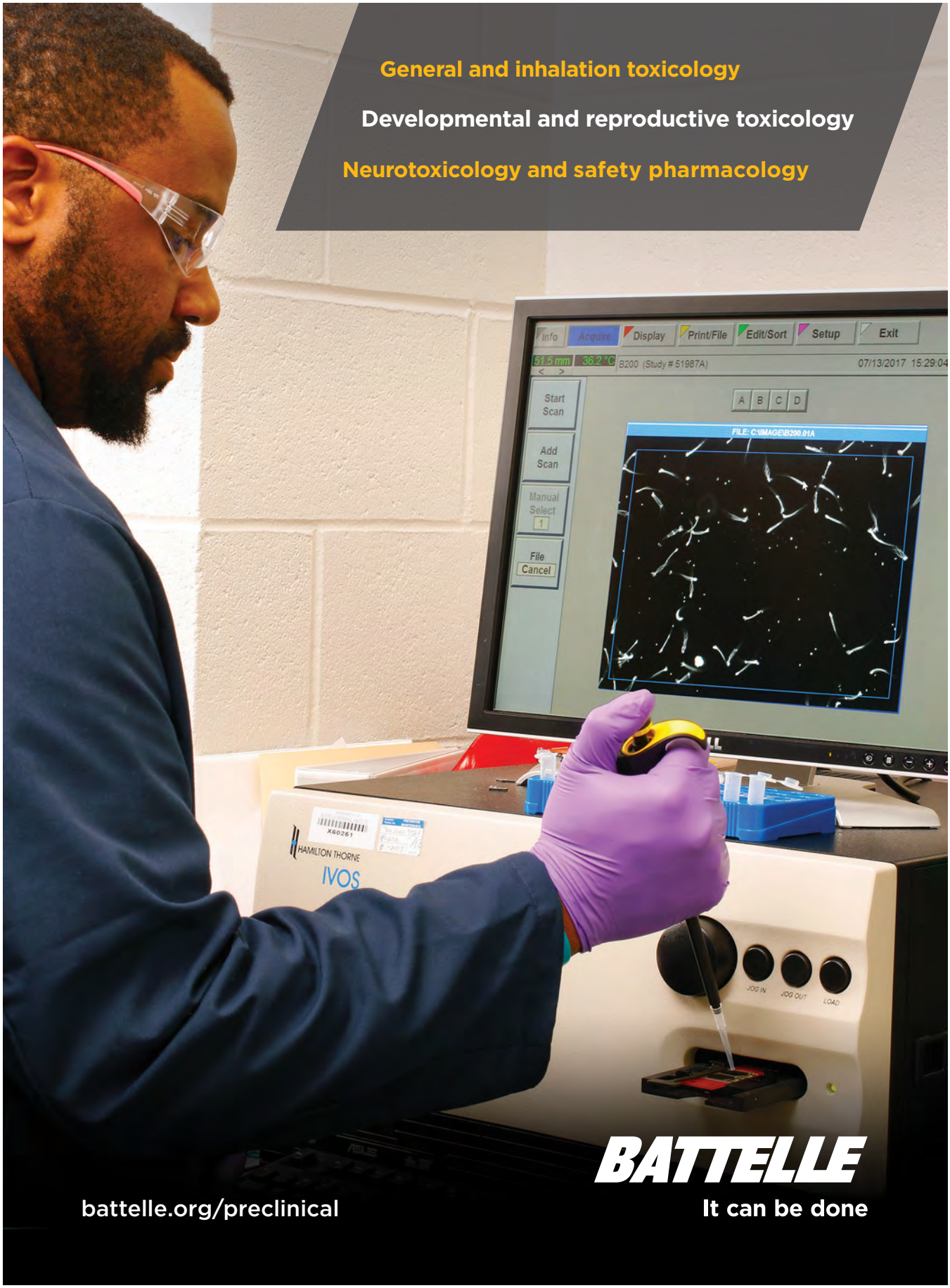
One speaker will present cardiotoxicity investigations of iPS-derived cells with optogenetic stimulation for efficient risk evaluation. A second will discuss *in vitro* methodologies investigating the use of adjuvant chemotherapy to prevent tumor recurrence. A third, by Coyne Scientific, will describe the use of a cohort of genetically-diverse iPS cardiomyocytes to assess toxicity.

High-Throughput Transcriptomics: Addressing the Human Risk Assessment Challenges of Chemical Coverage, Metabolism, and Population Variation

Monday, March 12, 3:00 PM to 4:00 PM

Presented by: *BioSpyder Technologies*

In vitro approaches to chemical risk assessment are being more widely used for evaluating mechanisms of action and estimating effect doses. Several challenges remain before wide acceptance in regulatory settings. This session will cover topics such as coverage in chemical and biological space, lack of metabolic capacity, and understanding of population variability.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Strategies for Successful PreIND and IND Submissions for the Toxicologist

Monday, March 12, 3:00 PM to 4:00 PM

Presented by: *ToxStrategies*

Preparing PreINDs and INDs can be challenging. ToxStrategies consultants will provide strategic scientific and regulatory advice on preparing PreIND and subsequent IND submissions. Insights on the PreIND/IND process, addressing what nonclinical data to include, how to prepare concise nonclinical summaries, and how to avoid submission delays will be presented.

What Can *In Vitro* Toxicology Learn from Genetic Toxicology for Regulatory Acceptance?

Monday, March 12, 3:00 PM to 4:00 PM

Presented by: *Charles River and Toxys*

Acceptance of *in vitro* toxicology models has been slow or they have been difficult to adopt, despite formal validation and Organisation for Economic Co-operation and Development (OECD) test guidelines. What can *in vitro* toxicology learn from the genetic toxicology experience for the acceptance of these models and replacement of their, usually, acute tests?

Tuesday

A Novel 3D Microtissue-Based Platform for Studying Liver Fibrosis

Tuesday, March 13, 9:00 AM to 10:00 AM

Presented by: *InSphero Inc.*

This session will share the characterization of a 3D Human Liver Fibrosis Model as a novel tool to study liver fibrosis, suitable for high-throughput efficacy testing of anti-fibrotic drugs. The disease model consists of only primary cell material for more physiologically-relevant screening hits.

Advanced Therapy Medicinal Products—The Good, the Bad, and the Unknown

Tuesday, March 13, 9:00 AM to 10:00 AM

Presented by: *Envigo*

The nonclinical safety assessment of advanced therapies (cell and gene therapies) requires additional investigations beyond what is expected for traditional therapeutics. Frequently, the use of non-standard toxicology models, such immunodeficient rodent strains, is required to obtain crucial information on potential toxicities and inform clinical study design.

Are Your Regulatory Submission Timelines at Risk?

Tuesday, March 13, 9:00 AM to 10:00 AM

Presented by: *PDS Life Sciences*

The SEND (Standard for Exchange of Nonclinical Data) requirements have begun to roll out. The data standardization schema presents both challenges and opportunities for the toxicology community. This session will present the latest updates to the SEND requirements and the current best practices to comply with them for toxicologists.

TSCA Reform: Use of New Tools and Technology for Prioritization and Chemical Risk Evaluation

Tuesday, March 13, 9:00 AM to 10:00 AM

Presented by: *ToxStrategies, Inc.*

This session will provide an overview of chemical prioritization and risk evaluations under TSCA as amended by the Lautenberg Chemical Safety Act. It will focus on new analytical tools, technologies, and databases that can be used for prioritization and testing of new chemicals and for risk evaluation of existing chemicals.

Achieve Higher Quality Data and Enable Multiplexing Options by Adopting Real-Time *In Vitro* Cytotoxicity Assays in 2D/3D Cultures

Tuesday, March 13, 10:30 AM to 11:30 AM

Presented by: *Promega Corporation*

Real-time assay methods have been developed enabling kinetic measurement of live, dead, and apoptotic cells repeatedly from the same sample using a plate reader. The methods simplify and reveal how time and dose affect cytotoxicity in 2D or 3D models and enable downstream applications with the same samples.

Quantitative Methods for Monitoring Thyroid Hormones in Late-Fetal and Early-Neonatal Rat Specimens

Tuesday, March 13, 10:30 AM to 11:30 AM

Presented by: *Charles River*

During thyroid development in the late stages of gestation, serum concentrations of T3 and T4 can be well below the limits of detection using conventional assays. An HPLC/MS/MS method has been validated to secure accurate data during early development to meet the expectations of US Environmental Protection Agency (US EPA) and Organisation for Economic Co-operation and Development (OECD) guidelines.

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Quantitation of Oligonucleotides Using a Hybridization Method in Various Tissues and Species for Accurate Pharmacology and Toxicology Evaluations

Tuesday, March 13, 10:30 AM to 11:30 AM

Presented by: *Altasciences Clinical Research*

Antisense oligonucleotides (ASOs) are widely used for silencing gene expression leading to promising treatment of rare diseases. This session will be an introduction to concepts and techniques in support of ASOs quantitation in blood and various tissue samples. Case studies highlighting scientific considerations and regulatory challenges will be presented.

Three-Dimensional (3D) Cultures of HepaRG Cells Model Physiologically-Relevant Drug Metabolism, Drug-Induced Liver Injury, and Hepatic Signaling Pathways

Tuesday, March 13, 10:30 AM to 11:30 AM

Presented by: *Lonza*

Prediction of liver injury and toxicological mechanisms remain focal points to pharmacological and environmental toxicology research. In this presentation, the development and application of organotypic *in vitro* liver models (e.g., 3D) will be described, including their utility to predict liver injury and characterize physiologically-relevant transcriptomic perturbations reflective of human outcomes.

Development of Real-Time Cardiotoxicity and Hepaotoxicity Assays Using Human iPSC-Derived Cells

Tuesday, March 13, 12:00 Noon to 1:00 PM

Presented by: *ACEA Biosciences*

Human iPSC-derived cells provide a relevant model system for screening and assessment of potential toxicities associated with pharmaceutical and environmental compounds. In this session, the utility of real-time cell-based assay using matured iPSC-cardiomyocytes and iPSC-hepatocytes for risk assessment of pharmaceutical and environmental hazardous compounds will be discussed.

Solving Target Safety Assessment Challenges

Tuesday, March 13, 12:00 Noon to 1:00 PM

Presented by: *Instem*

Companies are under enormous pressure to quickly produce high-quality target risk assessments to make drug development decisions. KnowledgeScan (KS) Target Safety Assessment (TSA) is revolutionizing this area. Hear how Insterm clients are improving quality, reducing costs, getting faster results, and gaining value by engaging in TSA projects with Instem.

Telemetry and Data Production: Looking Beyond the Requirements

Tuesday, March 13, 12:00 Noon to 1:00 PM

Presented by: *emka TECHNOLOGIES Inc.*

Telemetry produces unprecedented volumes of recordings from which powerful software derives even larger volumes of results. This session will present the challenges and possible solutions for intelligent data analysis and handling big data: How to speed up analysis and processing, to report efficiently, and to mine information from various sources of historical data.

Let the Machine Do the Work: Using Automation for High-Throughput *In Vitro* Toxicity Assays

Tuesday, March 13, 12:00 Noon to 1:00 PM

Presented by: *Miltenyi Biotec Inc.*

Fast and standardized flow cytometry workflows overcome the limitations of microscopic analysis, providing both reproducible and reliable high content toxicology information. This session will present Litron Laboratories multiplexed DNA damage assay for MOA detection and the Institute for In Vitro Sciences efforts with flow cytometry and the human Cell Line Activation Test (h-CLAT).

Cardio *quick*Predict: A New Way to Evaluate the Cardiotoxicity Potential of Compounds

Tuesday, March 13, 1:30 PM to 2:30 PM

Presented by: *Stemina Biomarker Discovery, Inc.*

Stemina has developed a new cardiotoxicity assay, Cardio *quick*Predict, which predicts the cardiotoxicity potential of a compound based on changes in human iPSC-derived cardiomyocyte metabolism and viability and indicates whether the cardiotoxicity profile is consistent with functional or structural toxicity. This session will cover assay development, performance, and application.

WEDNESDAY

From Nose to Tail: Nonclinical Safety Assessment Success Factors in Rats

Wednesday, March 14, 9:00 AM to 10:00 AM

Presented by: *Envigo*

The rat has been used extensively in nonclinical safety assessment for many years. Rat strain and diet selection for long-term studies are important in mitigating age-related pathologies. Managing body weight, maintaining proper organ function, and avoiding non-nutrient confounders can impact animal welfare and should be considered when designing studies.

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Classic, Modern, and Innovative Uses of Electron Microscopy in a GLP Environment

Wednesday, March 14, 10:30 AM to 11:30 AM

Presented by: *Charles River*

Electron microscopy (EM) has evolved as generations of scientists have pushed the boundaries of its classical application to answer novel scientific questions. Experience demonstrates that EM can be successfully utilized in a good laboratory practice (GLP) regulatory environment for a variety of important applications in discovery, safety assessment, and manufacturing.

Designed-for-Purpose: Complex Liver Cell Cultures for Improving *In Vitro* Hepatotoxicity Testing

Wednesday, March 14, 10:30 AM to 11:30 AM

Presented by: *Lonza*

Lonza, in collaboration with ScitoVation, will present 2D and 3D hepatotoxicity models that can recapitulate *in vivo* liver phenotypes. These models combine primary hepatocytes and liver nonparenchymal cells to improve hepatocyte viability, phenotype, and response to chemicals. Maximizing improvements to phenotypic relevance while minimizing culture complexity will be discussed.

Ensuring SEND Success beyond Regulatory Compliance

Wednesday, March 14, 4:30 PM to 5:30 PM

Presented by: *Instem*

SEND—is it simply a standard, or are there more commercial factors that organizations are overlooking? Join us for this informative session where we will be discussing how to exploit the standard beyond simply being compliant. During this time attendees will also receive the latest SEND updates.

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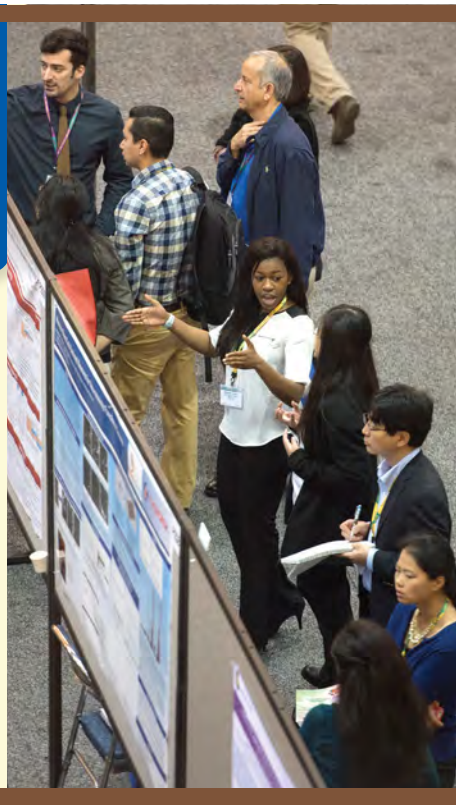

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